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A history of muscle physiology, Volume III: 1900 to 1960

CHAPTER 1

CERTAIN MATHEMATICAL CONCEPTS I. ORTHOGONALITY OF PRINCIPLE OSCILLATIONS OR MODES OF A VIBRATING SYSTEM.

A certain relationship between functions, known as an orthogonal relationship, is very useful in bio-mathematics. It can be described as follows:

Given two functions of x, or $f_n(x)$ and $f_m(x)$. These two functions are defined as orthogonal through the range a to b if the integral of their product equals zero:

$$\int_a^b f_n(x)\ f_m(x)\,dx = 0$$

where $m \neq n$.

The word orthogonal comes from vector analysis, where two vectors A and B are said to be orthogonal if $A \cdot B = A_x B_x + A_y B_y + A_z B_z = 0$. In like manner, vectors with n dimensions having exponents A_i, B_i ($i = 1, 2, \ldots, n$) are orthogonal when

$$\sum_{i=1}^{i=n} A_i A_i = 0.$$

In a vector space of infinite number of dimensions, with components $A_i \infty B_i$ continuously distributed, over the range 0 to s:

$$\int_0^s A(x)\,B(x)\,dx = 0.$$

Consider now the differential equation for a vibrating cantilever beam of uniform cross section:

$$EI\frac{d^4y}{dx^4} = -\,m\frac{d^2y}{dt^2} \qquad (1.1)$$

where E = Youngs' modular of elasticity

I = moment of inertia of x-sec of beam at x

x = distance on beam from support where x = 0

y = deflection of beam at x

m = mass of beam per unit length.

Assume that the beam shows a harmonic force vibration at a frequency ω, so that

$$y(x, t) = y(x) \sin \omega t.$$

then, since

$$m \frac{d^2y}{dt^2} + ky = 0$$

$$\frac{d^2y}{dt^2} + \frac{k}{m} y = 0$$

$$\text{and } \omega = \sqrt{\frac{k}{m}}, \quad \omega^2 = \frac{k}{m}$$

$$\frac{d^2y}{dt^2} = -\omega^2 y \tag{1.2}$$

Substituting (1.2) for (1.1) gives

$$EI \frac{d^4y}{dx^4} = m\omega^2 y$$

$$\text{or } (EIy'')'' = m\omega^2 y \tag{1.3}$$

A vibrating beam has many modes of oscillation, so that (1.3) can be written for two different modes, n and m:

$$(EIy_n'')'' = m\omega_n^2 y_n \tag{1.4}$$

$$\text{and } (EIy_m'')'' = m\omega_m^2 y_m \tag{1.5}$$

If (1.4) is multiplied by y_m and (1.5) by y_n, and if then (1.5) is subtracted from (1.4) and the result integrated over the length L of the beam, then:

$$\int_0^L \left[y_m (EI y_n'')'' - y_n (EI y_m'')'' \right] dx = \int_0^L m (\omega_n^2 y_m y_n - \omega_m^2 y_m y_n)\, dx \qquad (1.6)$$

$$= (\omega_n^2 - \omega_m^2) \int_0^L m y_n y_m \, dx$$

Note in the equation (1.6), that if the principle of orthogonality holds for modes of vibration, then

$$\int_0^L m y_n y_m \, dx = 0 \qquad (1.7)$$

where $m \neq n$.

Equation (1.7) can be shown to be valid by integrating the left hand side of the equation (1.6) by parts:

$$\int_0^L \left[y_m (EI y_n'')'' - y_n (EI y_m'')'' \right] dx \qquad (1.8)$$

Recall that in integration by parts:

$$\int u dv = uv - \int v du$$

Hence, let

$$y_m = u_1 \quad , \quad \text{thus } du_1 = y_m'$$

$$(EI\, y_n'')'' = dv_1 \quad , \quad \text{thus } v_1 = (EI\, y_n'')'$$

$$y_n = u_2 \quad , \quad \text{thus } du_2 = y_n'$$

$$(EI\, y_m'')'' = du_2 \quad , \quad \text{thus } v_2 = (EI\, y_m'')'$$

and (1.8) becomes:

$$\left[y_m (EI\, y_n'')' \right]_0^L - \int_0^L (EI\, y_n'')' y_m \, dx - \left[\left[y_n (EI\, y_m'')' \right]_0^L - \int_0^L (EI\, y_m'')' y_n' \, dx \right]$$

or

$$\left[y_m (EI\, y_n'')' - y_n (EI\, y_m'')' \right] - \int_0^L \left[(EI\, y_n'')' y_m' - (EI\, y_m'')' y_n' \right] dx \qquad (1.9)$$

For many boundary conditions, the first term, in brackets, of (1.9) is zero. For example, in a cantilever beam, the shear force, $S = EI\, y'''$, at the end of the beam is zero.

Hence, equation (1.8) reduces to

$$-\int_0^L \left[(EI\, y_n'')' - (EI\, y_n'')'\, y_n' \right] dx \tag{1.10}$$

This equation can again be integrated by parts, letting

$$y_m' = u, \qquad du = y_m''$$

$$(EI\, y_n'')' = dv, \qquad v = EI\, y_n''$$

and

$$y_n' = u, \qquad du = y_n''$$

$$(EI\, y_m'')' = dv, \qquad v = EI\, y_n''$$

giving

$$-\left\{ y_m' (EI\, y_n'') - \int_0^L (EI\, y_n'')\, y_m''\, dx - \left[y_n' (EI\, y_m'') - \int_0^L (EI\, y_m'')\, y_n''\, dx \right] \right\}$$

$$\left[y_n' (EI\, y_m'') - y_m' (EI\, y_n'') \right] + \int_0^L \left[(EI\, y_n'')\, y_m'' - (EI\, y_m'')\, y_n'' \right] dx$$

In this equation, the moment at the end of the beam, $M = EI\, y''$, is zero, so that the first term, in brackets, drops out. Also it is obvious that

$$\int_0^L (EI\, y_n''\, y_m'' - EI\, y_n''\, y_m'')\, dx \equiv 0 \quad \text{(identically zero)}.$$

Thus, the entire left hand side of equation (1.6) = 0, and therefore

$$(\omega_n^2 - \omega_n^2) \int_0^L m\, y_n\, y_m\, dx = 0$$

since $n \neq m$, and $\omega_n \neq \omega_m$,

$$\omega_n^2 - \omega_n^2 \neq 0, \text{ so that}$$

$$\int_0^L m\, y_n\, y_m\, dx = 0.$$

This, by definition, is the principle of orthogonality, and has herein been proved for the modes of a vibrating beam.

CHAPTER 2

CERTAIN MATHEMATICAL CONCEPTS II. PARTIAL DIFFERENTIAL EQUATIONS; THE WAVE EQUATION.

Ordinary differential equations describe relations between one dependent and one independent variable. Partial differential equations describe relations between a dependent variable and any number of independent variables. The vibrating string problem will serve as an example.

Let a string be stretched between two points, $x = 0$ and $x = L$, on the x axis (Figure 2.1). At $t = 0$ the string is pulled up at the middle, $x = 1/2\ L$, to a distance h, and released. The problem is to describe mathematically the subsequent motion.

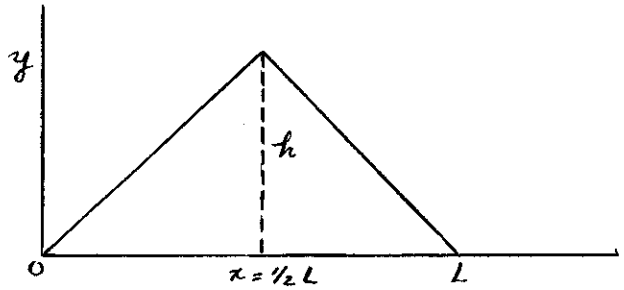


FIGURE 2.1. Vibrating string problem at $t = 0$.

Assume that at time t the string has the shape indicated in Fig. 2.2.

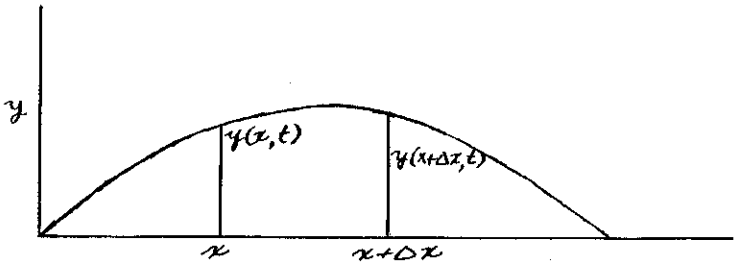


FIGURE 2.2. Vibrating string problem at $t = t$. Hence the displacement at x is $y(x, t)$, and at $x + \Delta x$ is $y(x + \Delta x, t)$.

Consider the forces acting on the element of string between x and $x + \Delta x$. There are two forces, the tension $T(x)$ pulling on the element to the left, and the tension $T(x + \Delta x)$ pulling on the element from the right. It is assumed that the tension is a function of x.

These forces are resolved into components as follows (Figure 2.3):

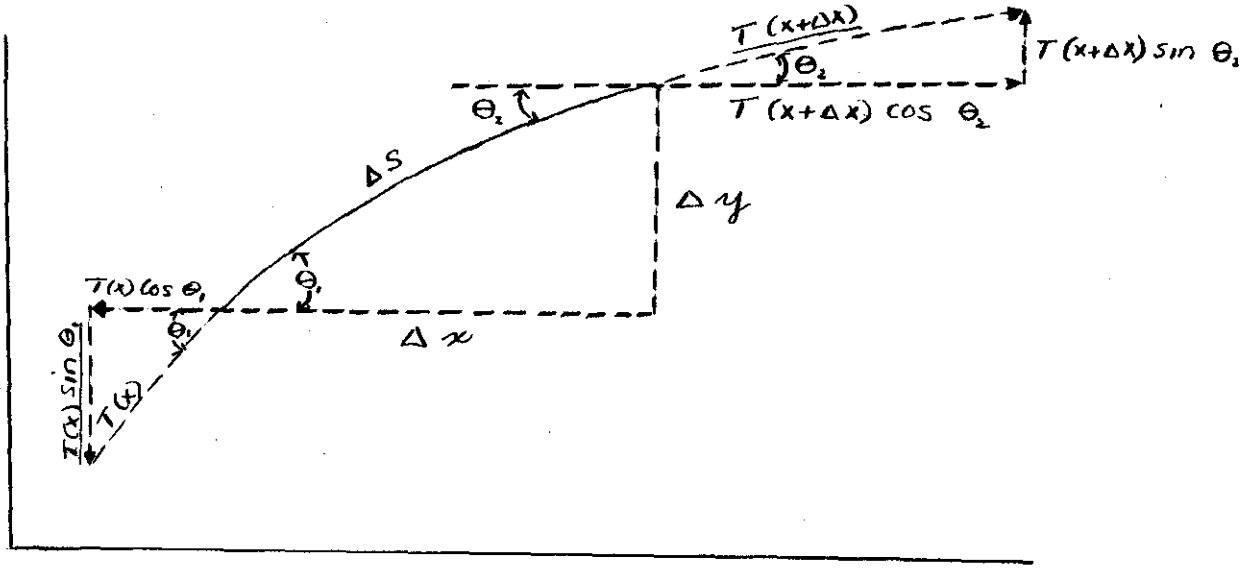
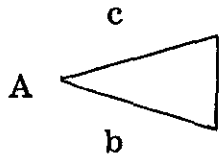


FIGURE 2.3. Forces acting on segment of string.

Recall that if  , then $\sin A = \frac{a}{c}$, $\cos A = \frac{b}{c}$.

Hence, net vertical or upward force = $T(x + \Delta x) \sin \theta_2 - T(x) \sin \theta_1$.
Net horizontal force, to right = $T(x + \Delta x) \cos \theta_2 - T(x) \cos \theta_1$.

If the string has a mass p/unit length, then the mass of the element is $p\Delta S$. The net vertical acceleration of the element is $\frac{\partial^2 y}{\partial t^2}$. From Newton's law it follows that

$$T(x + \Delta x) \sin \theta_2 - T(x) \sin \theta_1 = p\Delta S \frac{\partial^2 y}{\partial t^2} . \qquad (2.1)$$

If θ is the angle which a tangent makes with the x axis to any point on the string, then θ is a function of x, and

$$\theta_1 = \theta(x), \qquad \theta_2 = \theta(x + \Delta x)$$

Substituting these values into (2.1), and dividing by Δx, gives:

$$\frac{T(x + \Delta x) \sin \theta (x + \Delta x) - T(x) \sin \theta (x)}{\Delta x} = p \frac{\Delta S}{\Delta x} \frac{\partial^2 y}{\partial t^2} \qquad (2.2)$$

For very small elements of the string, and for very small displacements, it follows that ΔS will approximate Δx, or $\frac{\Delta S}{\Delta x} \simeq 1$. Also, since

$\tan\theta = \frac{a}{b}$, and $\sin\theta = \frac{a}{c}$, for small angles of θ, $b \cong c$, and $\sin\theta\,(x)$ can be replaced with $\tan\theta\,(x)$, and $\sin\theta\,(x + \Delta x)$ replaced with $\tan\theta\,(x + \Delta x)$. Thus, equation (2.2) can be written as

$$\frac{T\,(x + \Delta s)\tan\theta\,(x + \Delta x) - T(x)\tan\theta\,(x)}{\Delta x} = p\,\frac{\partial^2 y}{\partial t^2} \tag{2.3}$$

Taking the limit, as $\Delta x \to 0$, as follows:

let $y = f(x)$

where $y = T(x)\tan\theta\,(x) = f(x)$

Since $y + \Delta y = f(x + \Delta x)$

and $\Delta y = f(x + \Delta x) - f(x)$

and $$\frac{\Delta y}{\Delta x} = \frac{f(x + \Delta x) - f(x)}{\Delta x} \tag{2.4}$$

which, when $\Delta x \to 0$,

$$\lim_{\Delta x \to 0} \quad \frac{\Delta y}{\Delta x} = \frac{dy}{dx}$$

Note that the left hand side of equation (2.3) is the same as the right hand side of equation (2.4). Taking the limit of (2.3) therefore, gives on the left hand side

$$\frac{dy}{dx}, \text{ where } y = T(x)\tan\theta\,(x), \text{ or}$$

$$\frac{d}{dx}\Big(T(x)\tan\theta\,(x)\Big).$$

Hence equation (2.3) becomes

$$\frac{\partial}{\partial x}\Big[\,T(x)\tan\theta\,(x)\,\Big] = p\,\frac{\partial^2 y}{\partial t^2} \tag{2.5}$$

and since $\tan\theta(x) = \frac{\partial y}{\partial x}$, (2.5) becomes

$$\frac{\partial}{\partial x}\Big[\,T(x)\,\frac{\partial y}{\partial x}\,\Big] = p\,\frac{\partial^2 y}{\partial t^2} \tag{2.6}$$

If $T(x) = T$, a constant, then (2.6) can be written as

$$T\,\frac{\partial^2 y}{\partial x^2} = p\,\frac{\partial^2 y}{\partial t^2} \tag{2.7}$$

or, setting $\frac{T}{p} = a^2$, (2.7) becomes

$$\frac{\partial^2 y}{\partial t^2} = a^2 \frac{\partial^2 y}{\partial x^2} \tag{2.8}$$

Equations 2.6, 2.7, and 2.8 are various forms of the vibrating string equation, or more commonly, the wave equation.

In solving this equation for the vibrating string problem, assume T = constant. The boundary conditions of the problem are as follows:

Since the string is fixed at points x = 0 and x = L, the displacement y at these points is 0:

$y(0, t) = 0$, $y(L, t) = 0$ for $t \geq 0$.

Also, since the displacemèmt at t = 0 and x = 1/2 L was h,

$$y(x, 0) = \frac{2hx}{L} \qquad 0 \leq x \leq \frac{L}{2}$$

and

$$y(x, 0) = \frac{2h}{L}(L - x) \qquad \frac{L}{2} \leq x \leq L.$$

These are the equations for the straight line portions of Figure 2.1.

Since the string is released from rest, the initial velocity at all points is zero:

$$\frac{\partial y}{\partial t}(x, 0) = y_t(x, 0) = 0.$$

In summary, the equation to solve is

$$\frac{\partial^2 y}{\partial t^2} = a^2 \frac{\partial^2 y}{\partial x^2}$$

with the boundary conditions:

$y(o, t) = 0$, $y(L, t) = 0$ for $t \geq$

$$y(x, 0) = \frac{2Lx}{L}, \quad 0 \leq x \leq \frac{L}{2}$$

$$y(x, 0) = \frac{2L}{L}(L - x), \quad \frac{L}{2} \leq x \leq L$$

$$y_t(x, 0) = 0$$

CHAPTER 2

CERTAIN MATHEMATICAL CONCEPTS III. INTRODUCTION TO THE SOLUTION OF THE WAVE EQUATION.

In the preceeding chapter, a wave equation was developed. Consider now a specific example of such an equation.

A string of length 2 feet, weighing 4 oz., is stretched with a tension of 1 lb. force throughout. The center of the string is raised 1/4 inch above the equilibrium position and released. Let it be required to find the subsequent displacement of the string or a function of time and distance from the ends which are fixed.

The general wave equation for the string is

$$\frac{\partial^2 y}{\partial t^2} = a^2 \frac{\partial^2 y}{\partial x^2},$$

where $a^2 = \frac{T}{p}$, T = tension, p = mass/unit length. In this problem T = 1, $p = \frac{m}{1} = \frac{w}{lg} = \frac{1/4}{2.32} = \frac{1}{256}$, $a^2 = 256$, so that

$$\frac{\partial^2 y}{\partial t^2} = 256 \frac{\partial^2 y}{\partial x^2} \tag{3.1}$$

The boundary conditions are:

$$y(0, t) = 0, \qquad y(L, t) = 0 \quad \text{for } t \geq 0$$

$$y(x, 0) = \frac{2hx}{L}, \quad 0 \leq x \leq \frac{L}{2}$$

$$y(x, 0) = \frac{2h}{L}(L - x), \quad \frac{L}{2} \leq x \leq L$$

$$y_t(x, 0) = 0$$

and since L = 2, h = 1/48

$$y(0, t) = 0 \qquad y(2, t) = 0$$

$$y(x, 0) = \frac{1}{48} x \qquad 0 \leq x \leq 1$$

$$y(x, 0) = \frac{1}{48}(2 - x) \quad 1 \leq x \leq 2$$

Assume that a solution of equation (3.1) is a function of x, X, multiplied by a function of t, T, or

$$y = XT.$$

Differentiating twice with respect to t gives

$$\frac{dy}{dt} = X\frac{dT}{dt}$$

$$\frac{d^2y}{dt^2} = X\frac{d^2T}{dt^2} = XT''$$

Substituting XT'' into equation (3.1) for $\frac{\partial^2 y}{\partial t^2}$ gives

$$XT'' = 256\frac{\partial^2 y}{\partial x^2}$$

But $\frac{\partial^2 y}{\partial x^2}$ can be rewritten as

$$\frac{\partial^2 (XT)}{\partial x^2} = X'' T, \text{ and hence}$$

$$XT'' = 256\, X''\, T$$

and

$$\frac{T''}{256\,T} = \frac{X''}{X} = -\lambda^2 \tag{3.2}$$

Equation (3.1) has therefore been rewritten in terms of X and T.

Equation (3.2) can be separated into two equations:

$$T'' = -256\,\lambda^2 T \tag{3.3}$$

and

$$X'' = -\lambda^2 X \tag{3.4}$$

Recall that these equations are of the type

$$\ddot{y} + cy = 0,$$

which has a solution:

$$y = A\cos\sqrt{C}\ t + B\sin\sqrt{C}\ t$$

or

$$y = c_1 ie^{ix} - C_2 ie^{-ix}.$$

Consider the following as proof.

Given $\ddot{y} + y = 0$

If $y = A\cos t + B\sin t$

then $\dot{y} = -A\sin t + B\cos t$

and $\ddot{y} = -A\cos t - B\sin t.$

Hence, $\ddot{y} + y = -A \cos t - B \sin t + A \cos t + B \sin t = 0.$

Therefore, equation (3.3), $T'' + 256 \lambda^2 T = 0$ has the solution

$$T = C_1 \cos 16 \lambda t + D_1 \sin 16 \lambda t$$

and equation (3.4) has the solution

$$X = A_1 \cos 2x + B_1 \sin \lambda x.$$

Thus, if $y = XT$, then

$$y = (A_1 \cos \lambda x + B_1 \sin \lambda x)(C_1 \cos 16\lambda t + D_1 \sin 16 \lambda t) \qquad (3.5)$$

From the boundary conditions $y(0, t) = 0$,

$$y_{x=0} = (A_1 \cos 0 + B_1 \sin 0)(C_1 \cos 16 \lambda t + D_1 \sin 16 \lambda t)$$
$$= A_1 (C_1 \cos 16 \lambda t + D_1 \sin 16 \lambda t) = 0.$$

Hence, $A_1 = 0$ since the second factor cannot be zero and a solution still exist.

Substituting $A_1 = 0$ back into (3.5) gives:

$$y = \sin \lambda x (B_1 C_1 \cos 16 \lambda t + B_1 D_1 \sin 16 \lambda t).$$

Letting $B_1 C_1 = B$ and $B_1 D_1 = C$ gives

$$y = \sin \lambda x (B \cos 16 \lambda t + C \sin 16 \lambda t) \qquad (3.6)$$

From the boundary conditions $y(2, t) = 0$, (3.6) becomes:

$$y_{x=2} = \sin 2\lambda (B \cos 16 \lambda t + C \sin 16 \lambda t) = 0.$$

It is seen that $\sin 2\lambda = 0$ by necessity. Therefore, or since $\sin \pi = 0$, $\sin 2\pi = 0$, etc., we can write

$$\sin 2\lambda = 0 = \sin m\pi$$

where m = any integer. Hence $2\lambda = m\pi$, $\lambda = \frac{m\pi}{2}$.

Substituting this value of λ back into equation (3.6) gives

$$y = \sin \frac{m\pi x}{2} \quad (B \cos 8m\pi t + C \sin 8m\pi t) \qquad (3.7)$$

Consider now the boundary condition, $y(x, 0) = 0$. If (3.7) is differentiated with respect to t:

$$\frac{dy}{dt} = \sin \frac{m\pi x}{2} \quad (-B\, 8m\pi \sin 8\, m\pi t + C\, 8m\pi \text{ cps } 8m\pi t).$$

This expression is equal to zero at t = 0 from the boundary conditions, and also, at t = 0,

$$-B\, 8m\pi \sin 8m\pi t = 0$$

and

$$C\, 8m\pi \cos 8m\pi t = C\, 8m\pi.$$

Since $\sin \frac{m\pi x}{2}$ does not equal zero, $C\, 8m\pi = 0$, or more specifically, $C = 0$.

Hence (3.7) becomes:

$$y = B \sin \frac{m\pi x}{2} (\cos 8\, m\pi t). \tag{3.8}$$

At $t = 0$,

$$y = B \sin \frac{m\pi x}{2} \cos 8m\pi t = B \sin \frac{m\pi x}{2} \tag{3.9}$$

From the boundary conditions

$y(x, 0) = \frac{1}{48} x \qquad 0 \leq x \leq 1$, and

$y(x, 0) = \frac{1}{48} (2 - x) \qquad 1 \leq x \leq 2$,

equation (3.9) is written as

$$y_{t=0} = B \sin \frac{m\pi x}{2} = \frac{1}{48} x \qquad 0 \leq x \leq 1$$

and

$$y_{t=0} = B \sin \frac{m\pi x}{2} = \frac{1}{48} (2 - x) \quad 1 \leq x \leq 2.$$

These above two equations must be satisfied through the proper selection of m and x. However, it is not obvious how the selection should be made; therefore consider the following:

If U_1 and U_2 are two solutions of a differential, the $a_1 U_1 + a_2 U_2$ is also a solution, where a_1 and a_2 are any constants. For example, let

$$y = U_1 \qquad y = U_2$$

then

$$a_3 y = a_3 U_1 \qquad a_4 y = a_4 U_2$$

$$a_3 y + a_4 y = a_3 U_1 + a_4 U_2$$

$$y (a_3 + a_4) = a_3 U_1 + a_4 U_2$$

$$y = \frac{a_3}{a_3 + a_4} U_1 + \frac{a_4}{a_3 + a_4} U_2$$

Letting $\frac{a_3}{a_3 + a_4} = a_1$ and $\frac{a_4}{a_3 + a_4}$, then $y = a_1 U_1 + a_2 U_2$.

Likewise, if $U_1, U_2, \ldots U_n$ are solutions to an equation, then $a_1 U_1 + a_2 U_2 + \ldots a_n U_n$ is also a solution.

Therefore, if in equation (3.8), m is set equal to 1, 2 . . . . , and B at m = 1 equal to b_1, B at m = 2 to b_2, etc., then a solution for the original equation can be written, from (3.8), based on this principle of superposition,

as follows:

$$y(x,\ t) = b_1 \sin \frac{\pi x}{2}\ (\cos 8\pi t) + b_2 \sin \pi x\,(\cos 16\ \pi t) + \ldots . \qquad (3.10)$$

Note that at t = 0, (3.10) becomes

$$y(x,\ 0) = b_1 \sin \frac{\pi x}{2} + b_2 \sin \pi x \ldots . \qquad (3.11)$$

With this equation it is possible to satisfy the boundary conditions $y(x,\ 0) = \frac{1}{48}x$ or $\frac{1}{48}(2 - x)$, with proper choice of b_1, b_2, etc.

In order to solve equation (3.10), and to find a complete solution to the problem, the constants b_1, b_2, etc. must be evaluated. The technique used for the evaluation is Fourier analysis, and is the subject of the next chapter.

CHAPTER 4

CERTAIN MATHEMATICAL CONCEPTS IV. FOURIER SERIES AND FINAL SOLUTION OF THE WAVE EQUATION.

In the general series,

$$A + a_1 \cos \frac{\pi x}{L} + a_2 \cos \frac{2\pi x}{L} + \ldots . \; b_1 \sin \frac{\pi x}{L} + b_2 \sin \frac{2\pi x}{L} + \ldots . = f(x),$$

where L = length of system in motion = $\frac{1}{2}$ period of vibration and A, a_1, a_2, b_1, b_2, etc. = constants, Fourier found that:

$$A = \frac{1}{2L} \int_{-L}^{L} f(x)\, dx.$$

$$a_k = \frac{1}{L} \int_{-L}^{L} f(x) \cos \frac{k\pi x}{L}\, dx.$$

$$b_k = \frac{1}{L} \int_{-L}^{L} f(x) \sin \frac{k\pi x}{L}\, dx$$

where k = 1, 2, 3. . . . .

If the series contains only sine terms, as in a Fourier sine series (also called an odd function), as

$$f(x) = b_1 \sin \frac{\pi x}{L} + b_2 \sin \frac{2\pi x}{L} + \ldots .$$

then $A = 0$

$$a_k = 0$$

$$b_k = \frac{2}{L} \int_{0}^{L} f(x) \sin \frac{k\pi x}{L}\, dx$$

If the series contains only cosine terms, a Fourier cosine series, or an even function:

$$f(x) = A + a_1 \cos \frac{\pi x}{L} + a_2 \cos \frac{2\pi x}{2} + \ldots .$$

then $$A = \frac{1}{L} \int_{0}^{L} f(x)\, dx$$

$$a_k = \frac{2}{L}\int_0^L f(x)\cos\frac{k\pi x}{L}\,dx$$

$$b_k = 0.$$

Consider now equations (3.10) and (3.11). From (3.11), a Fourier sine series, it is apparent that

$$b_k = \frac{2}{2}\int_0^2 y\,(x,\ 0)\sin\frac{k\pi x}{2}\,dx \qquad (4.1)$$

Note that the expression is integrated between the limits x = 0 and x = 2. Recall thay $y\,(x,\ 0) = \frac{1}{48}\,x$ at $0 \leq x \leq 1$ and $y\,(x,\ 0) = \frac{1}{48}\,(2 - x)$ at $1 \leq x \leq 2$. Hence (4.1) is rewritten as:

$$b_k = \int_0^1 \frac{x}{48}\sin\frac{k\pi x}{2}\,dx + \int_1^2 \frac{1}{48}\,(2 - x)\sin\frac{k\pi x}{2}\,dx$$

and

$$b_k = \frac{1}{48}\int_0^1 x\sin\frac{k\pi x}{2}\,dx + \frac{1}{24}\int_1^2 \sin\frac{k\pi x}{2}\,dx - \frac{1}{48}\int_1^2 x\sin\frac{k\pi x}{2}\,dx \qquad (4.2)$$

The three integrals of (4.2) are evaluated as follows:
The first integral is solved using the relation:

$$\int x\sin ax\,dx = \frac{1}{a^2}\,(\sin ax - ax\cos ax),$$

letting $\frac{k\pi}{2}$ represent a. Thus,

$$\frac{1}{48}\int_0^1 x\sin\frac{k\pi x}{2}\,dx = \frac{1}{48}\left[\frac{4}{k^2\pi^2}\left(\sin\frac{k\pi x}{2} - \frac{k\pi x}{2}\cos\frac{k\pi x}{2}\right)\right]_0^1$$

$$= \frac{1}{12k^2\pi^2}\sin\frac{k\pi}{2} - \frac{1}{24k\pi}\cos\frac{k\pi}{2}$$

The third integral is solved using the same principle:

$$-\frac{1}{48}\int_1^2 x\sin\frac{k\pi x}{2}\,dx = -\frac{1}{48}\left[\frac{4}{k^2\pi^2}\left(\sin\frac{k\pi x}{2} - \frac{k\pi x}{2}\cos\frac{k\pi x}{2}\right)\right]_1^2$$

$$= -\frac{1}{12k^2\pi^2}\sin k\pi + \frac{1}{12k\pi}\cos k\pi + \frac{1}{12k^2\pi^2}\sin\frac{k\pi}{2} - \frac{1}{24k\pi}\cos\frac{k\pi}{2}.$$

Since $\sin \pi$, $\sin 2\pi$, etc. $= 0$, the above reduces to

$$= \frac{1}{12k\pi}\cos k\pi + \frac{1}{12k^2\pi^2}\sin\frac{k\pi}{2} - \frac{1}{24k\pi}\cos\frac{k\pi}{2}.$$

The second integral is evaluated directly:

$$\frac{1}{24}\int_1^2 \sin\frac{k\pi x}{2}\,dx = \frac{1}{12k\pi}\cos\frac{k\pi}{2} - \frac{1}{12k\pi}\cos k\pi.$$

The solution of (4.2) therefore is the combination of the three solutions:

$$b_k = \frac{1}{12k^2\pi^2}\sin\frac{k\pi}{2} - \frac{1}{24k\pi}\cos\frac{k\pi}{2} + \frac{1}{12k\pi}\cos k\pi + \frac{1}{12k^2\pi^2}\sin\frac{k\pi}{2} - \frac{1}{24k\pi}\cos\frac{k\pi}{2} + \frac{1}{12k\pi}\cos\frac{k\pi}{2} - \frac{1}{12k\pi}\cos k\pi.$$

Note that in this solution the third and seventh terms cancel, the second and fifth terms combine and cancel the sixth term, and the first and fourth term combine giving:

$$b_k = \frac{1}{6k^2\pi^2}\sin\frac{k\pi}{2} \tag{4.3}$$

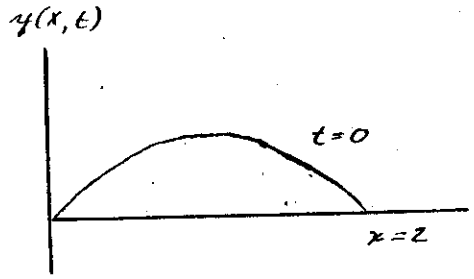
Also note that if k is even, then $b_k = 0$, and that if $k = 1$, $b_k = +$; $k = 3$, $b_k = -$, etc.

The value of b_k, (4.3), is now substituted into (3.10), setting $k = 1, 3, \ldots$, giving

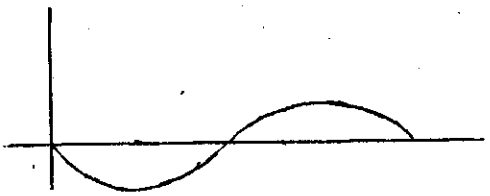
$$y(x, t) = \frac{1}{6\pi^2}\sin\frac{\pi x}{2}\cos 8\pi t - \frac{1}{6\cdot 3^2\pi^2}\sin\frac{3\pi x}{2}\cos 24\pi t + \frac{1}{6\cdot 3^2\pi^2}\sin\frac{5\pi x}{2}\cos 42\pi t - \ldots\ldots \tag{4.4}$$

Equation (4.4) represents the complete solution of the problem. Each term represents a particular mode of vibration of the system; the

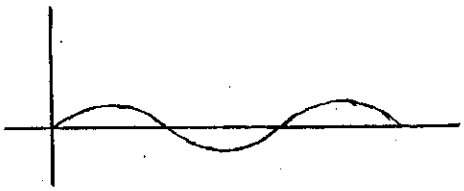
first term the first mode of vibration, etc. Thus, the first mode is:



described by $\sin \frac{\pi x}{2} \cos 8\pi t$. As t varies, the tendency is for the string to oscillate about the x axis in the pictured manner, at a frequency given by $\cos 8\pi t$ or 4 cycles/second. This is the lowest frequency of oscillation of the system and is called the fundamental frequency or first harmonic. Since $b_k = 0$ in (4.4) the second mode is absent. The third mode:



is given by $\sin \frac{3\pi x}{2} \cos 24\pi t$, the frequency being 12 cycles/second. The fourth mode is absent; the fifth:



has a frequency of 20 cycles/second. It is thus seen that all the harmonic frequencies are integer multiples of the fundamental; 4×3, 4×5, ... The coefficients of (4.4), $\frac{1}{6\pi^2}$, etc., measure the intensities of the modes, or the displacements from the x axis. Thus the higher frequencies have lower intensities. In carrying out solutions, calculation of the first three or four terms of (4.4) gives a good approximation of y (x, t).

CHAPTER 5

THE DIFFUSION EQUATION - DIFFUSION OF OXYGEN ACROSS CELL MEMBRANE

Oxygen molecules in solution are in constant motion by virtue of their kinetic energy. If the concentration of molecules is the same every place in the solution, no net transport of molecules from one region to another takes place. However, if in one region the concentration of the oxygen molecules is greater than in another, then there is a transport of oxygen from the first to the second region. The transfer process is termed diffusion, and is a passive physical process.

Consider a tube with a partition in the middle, separating water into two parts, one part containing dissolved oxygen, the other part free of oxygen. At the time T = 0, the concentration gradient of oxygen throughout the tube is sharply defined. The partition is now removed, and at t > 0 (T = t), the concentration gradient throughout the tube is found to be as illustrated in Figure 1. Diffusion of oxygen from one part of the tube to the other part has and is taking place.

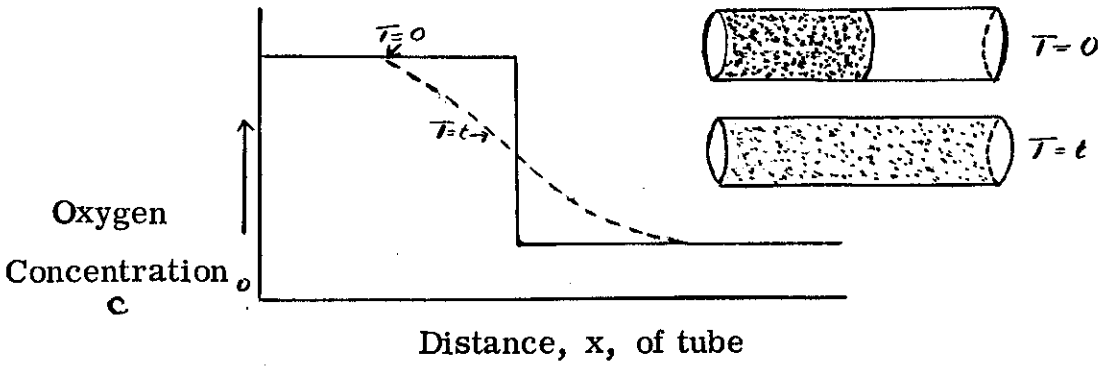


Figure 1. Concentration Gradients of O_2 at T = o and T = t.

The paths of motion of the oxygen molecules are random during the diffusion process, and the distribution of molecules at any one time can be predicted by probability theory. This distribution is given in Figure 1.

Probability theory also predicts that the concentration gradient of oxygen per unit of x is greatest in the region occupied by the partition at T = o, and then diminishes on either side of this region. The concentration gradient at every point on x is given by the slope of the curve in Figure 1, i.e., the first derivative of the curve. It is illustrated in Figure 2.

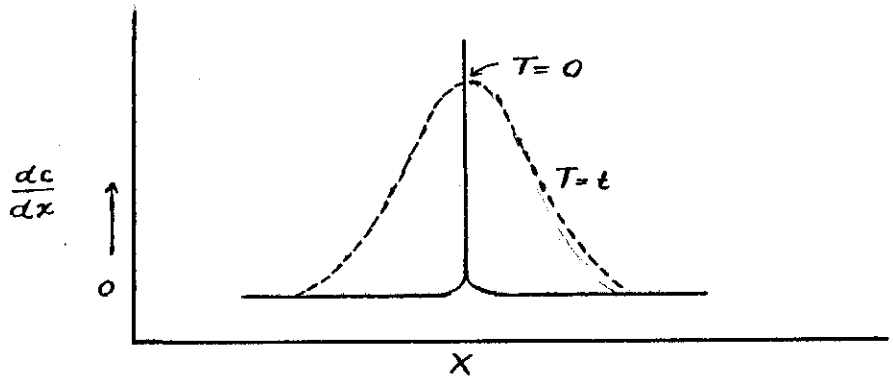


Figure 2. Concentration Gradient of Oxygen Along Cylinder.

The curve of Figure 2 is the bell-shaped Gaussian distribution curve, and simply demonstrates that the processes of diffusion are passive and random, and that they conform to probability theory.

The question may now be asked: How many oxygen molecules pass or diffuse through an area A per unit of time, at any point on x? It is reasonable to assume that the amount of oxygen which will diffuse through an area A will depend upon the concentration gradient across that area. In Figure 2, for example, at the ends of the curve where the concentration gradient is zero, i.e., $\frac{dc}{dx} = 0$, it would not be expected that any diffusion of oxygen would occur. On the other hand, it would be expected that the greatest amount of oxygen would diffuse at point of x where $\frac{dc}{dx}$ has the greatest value, in the center of the curve. Hence, the amount of oxygen, dn, diffusing through an area, A, per unit time, dt, can be said to be proportional (D = constant of proportionality, or the diffusion coefficient) to the concentration gradient, $\frac{dc}{dx}$, existing across A at time t.

In symbols:

$$\frac{dn}{dt} = - DA \left(\frac{dc}{dx} \right)_t . \qquad (5.1)$$

This is known as Fick's Law of Diffusion, which was stated in 1855 and which was subsequently proven experimentally. The constant of proportionality, D, is not really a constant, but changes with dilution of the solute and with temperature, which is to be expected since diffusion results from kinetic motion. The term, therefore, is more appropriately referred to as the diffusion coefficient. The minus sign of the equation indicates that diffusion is taking place from a region of higher concentration to a region of lower concentration. The slope of the distribution curve of Figure 1, or $\frac{dc}{dx}$, is always numerically negative.

Thus far the amount of oxygen, dn, diffusing per unit time, dt, has been considered as has the change in concentration of oxygen, dc, across a unit distance, dx.

It is also of interest to consider the change of concentration of oxygen, dc, at a point x during the time interval, dt, or $\frac{dc}{dt}$; the rate of change of concentration at point x.

If the point x is represented as an element of volume bounded by parallel planes of area A and separated by a distance dx, then the volume between the planes is represented by A dx. If the volume A dx is in a region of low concentration of oxygen, then with diffusion the concentration of oxygen within the volume will increase. Oxygen will accumulate within the volume; more oxygen will enter than will leave. During the time interval dt, let the amount of oxygen which enters the volume be dn, and the amount which leaves the volume be dn "plus" a small change in the amount dn, d(dn). This change would be negative, as a– 5 molecules of oxygen. Thus the amount which leaves can be written dn + d(dn). The amount of oxygen which accumulates in the volume is therefore dn – [dn + d(dn)] = – d(dn).

To express this amount in concentration terms, it is divided by the volume under consideration to $- d \frac{(dn)}{Adx}$. This represents the change in concentration of oxygen, dc, in the time period dt. The time rate of change of concentration, i.e., dc per dt, is given by:

$$\left(\frac{dc}{dt}\right)_x = - \frac{1}{Adt} \left(\frac{d(dn)}{dx}\right). \tag{5.2}$$

The term $\frac{d(dn)}{dx}$ can be evaluated by writing equation (5.1) as:

$$dn = - DA\ dt \left(\frac{dc}{dx}\right)_t .$$

which, after differentiation is:

$$\frac{d(dn)}{dx} = - DA\ dt \frac{(d^2 c)}{(dx^2)_t} \tag{5.3}$$

holding dt constant.

Substituting the right hand expression of equation (5.3) into equation (5.2) for $\left(\frac{d(dn)}{dx}\right)$ gives:

$$\left(\frac{dc}{dt}\right)_x = D \left(\frac{d^2 c}{dx^2}\right)_t . \tag{5.4}$$

Consider now an actively respiring plane of tissue exposed to an oxygenated solution on one surface. Consider that at time T = 0, no oxygen exists in the tissue; and that at time T = t, oxygen is diffusing into the tissue along a concentration gradient. The rate at which oxygen would accumulate in the tissue at point x is the time rate of change of concentration, $\left(\frac{dc}{dt}\right)_x$. However, in the steady state, at equilibrium, no more oxygen would accumulate, the rate at which it would accumulate being equal to the rate of oxygen consumption by the tissue, designated as "a". Hence,

$$\left(\frac{dc}{dt}\right)_x = a = D \left(\frac{d^2 c}{dx^2}\right)_t$$

or

$$\frac{d^2c}{dx^2} = \frac{a}{D} \tag{5.5}$$

Equation (5.5) is solved as follows:

Integrating once yields

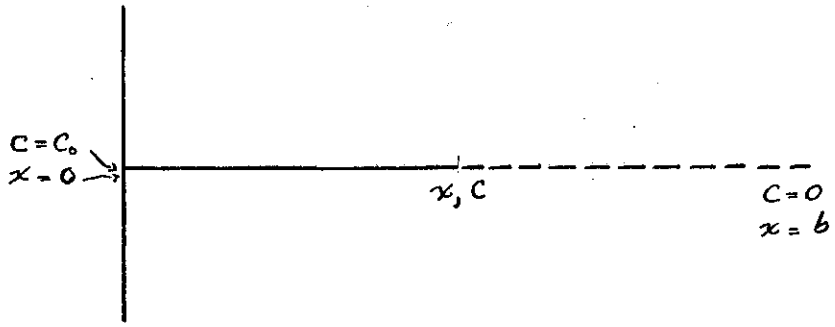
$$\frac{dc}{dx} = \frac{ax}{D} + B_1 .$$

Integrating again yields

$$c = \frac{ax^2}{2D} + B_1 x + B_2 . \tag{5.6}$$

B_1 and B_2 are constants of integration and are evaluated as follows:

Let C_o be the concentration of oxygen in the fluid outside of the tissue, the concentration being constantly maintained by perfusion or continuous oxygenation of the fluid. Let C then be the concentration of oxygen at any distance x perpendicular to the surface of the tissue. At the surface of the tissue, x = 0. Also, at a distance from the surface where C = 0, let x = b.



Now, let $c = 0$, and equation (5.6) reduces to

$$C_o = B_2$$

and B_2 is evaluated.

Next, setting x = b where C = 0, equation (5.6) becomes

$$0 = \frac{ab^2}{2D} + B_1 b + C_o \tag{5.7}$$

Differentiating (5.7) with respect to x = b,

$$0 = \frac{ab}{D} + B_1$$

Hence,

$$B_1 = -\frac{ab}{D}.$$

Thus, for the conditions where x = b and C = 0, equation (5.6) can be written:

$$0 = \frac{ab^2}{2D} - \frac{ab^2}{D} + C_o,$$

or,

$$C_o = \frac{ab^2}{2D}.$$

Solving for b,

$$b = \sqrt{\frac{2DC_o}{a}} \qquad (5.8)$$

Equation (5.8) therefore gives the thickness of the tissue at which oxygen concentration will be zeor. In practice, slices of tissue are placed in a medium where the oxygen diffuses into the tissue from both surfaces. Hence, the thickness, i.e., the width, d, of the tissue where the concentration of oxygen is just zero at the tissue center on a diffusion basis, will be twice the expression of equation (5.8).

$$d = 2\sqrt{\frac{2DC_o}{a}} = \sqrt{\frac{8DC_o}{a}} \qquad (5.9)$$

Equation (5.9) is Warburg's well known expression for determining the limiting thickness of a tussue which may be used for respiratory studies. The units for the terms of the equation, and an example of its usage, are as follows:

d = limiting thickness in cm.

D = diffusion coefficient for O_2, in ml/min/cm^2.

a = respiratory rate of tissue, in ml O_2 uptake/ml tissue/min.

C_o = O_2 concentration of medium outside tissue slice, in atm.

Suppose that in a given experiment, the respiration of liver slices is being measured. The rate of respiration is found to be 12 μl O_2 consumed

per mg. dry wt. of tissue, per hour; run under 100% O_2 (Q_{O_2}).

The value of the diffusion coefficient is taken from the work of Krogh, and equals 1.4×10^{-5} ml per minute of oxygen diffusing at 38°C through a tissue of 1 cm^2 cross section. Assume that the experiment is run at 38°C. The value of C_o is therefore 1 atm.. Converting the found Q_{O_2} for the liver tissue into ml/ml tissue/min:

$$\frac{12 \times 1000}{4 \times 1000 \times 60} = 0.05 \text{ ml } O_2 \text{ uptake/ml tissue/min.}$$

assuming a specific gravity for the tissue of 1, and a wet weight-dry weight ration of 4.

The value of the terms for equation (5.9) would be:

$$D = 1.4 \times 10^{-5}$$

$$a = 0.05$$

$$C_o = 1$$

and

$$d = \sqrt{\frac{8(1.4 \times 10^{-5})}{0.05}} = 4.73 \times 10^{-2} \text{ cm or } 0.47 \text{ mm.}$$

CHAPTER 6

BLOOD CONCENTRATION OF CONTINUOUSLY INFUSED X SUBSTANCE - DETERMINATION OF EXCRETION CONSTANT AND DISTRIBUTION SPACE.

Let a substance, x, be constantly infused at rate p mg/min. into the blood stream, and let it be distributed throughout the body fluids in volume V liters. If q = quantity of x substance in body, then its concentration c is $\frac{q}{V}$. Finally, let the rate of change of concentration of x substance be $\frac{dc}{dt}$, in mg/liter volume/unit time.

Then

$$\frac{dc}{dt_i} = p\,\frac{1}{V} \tag{6.1}$$

For example, if V = 10 liters and rate of infusion is 500 mg/minute, then the rate of change of concentration is $500 \times \frac{1}{10} = 50$ mg/liter/minute.

Assume that substance x is eliminated at a rate depending on its concentration:

$$\frac{dc}{dt_{(E)}} = -kc, \tag{6.2}$$

where k = velocity constant for excretion.

In the situation where infusion and excretion occur together, then equations (6.1) and (6.2) are combined:

$$\frac{dc}{dt} = \frac{p}{V} - kc \tag{6.3}$$

Equation (6.3) is solved as follows:

Write (6.3) or

$$\frac{dc}{dt} + kc = \frac{p}{V} \tag{6.4}$$

Hence, a solution is:

$$c = \frac{\frac{p}{V}}{k} + Z \tag{6.5}$$

and

$$\frac{dc}{dt} = \frac{dZ}{dt} \tag{6.6}$$

Using (6.5) and (6.6), equation (6.4) can be rewritten as:

$$\frac{dZ}{dt} + k\left(\frac{\frac{p}{V}}{k} + Z\right) = \frac{p}{V}$$

or

$$\frac{dZ}{dt} = -kZ$$

and

$$\frac{dZ}{Z} = -k\,dt.$$

Integrating,

$$\ln Z = -kt = c'$$

and

$$Z = Ce^{-kt}. \tag{6.7}$$

Substituting (6.7) into (6.5) gives

$$c = \frac{\frac{p}{V}}{k} + Ce^{-kt} \tag{6.8}$$

When $t = 0$, assume $c = 0$, and $C = -\frac{\frac{p}{V}}{k}$. Hence (6.8) is

$$c = \frac{p}{Vk} + \left(\frac{p}{Vk}\right)e^{-kt}$$

or

$$c = \frac{p}{Vk}\left(1 - e^{-kt}\right). \tag{6.9}$$

Equation (6.9) therefore gives the "blood" concentration of x substance at any time. If the distribution volume is unknown, then two measurements of blood concentration are necessary:

$$c_1 = \frac{p}{kV}\left(1 - e^{-kt_1}\right)$$

and

$$c_2 = \frac{p}{kV}\left(1 - e^{-kt_2}\right).$$

Hence

$$\frac{c_1}{c_2} = \frac{1 - e^{-kt_1}}{1 - e^{-kt_2}}$$

and

$$c_1 - c_2 = c_1 e^{-kt_2} - c_2 e^{-kt_1}$$

$$k = \frac{\ln (c_1 - c_2)}{c_2 t_1 - c_1 t_2}$$

With this value of k, the excretion constant, equation (6.9) can be solved for V. If $c \neq 0$ at $t = 0$, then it can be set equal to the concentration of x substance above that at $t = 0$.

CHAPTER 7

ANALYSIS OF THE ARTERIAL PULSE.

This chapter represents a first attempt to analyze the arterial pulse curve. The analysis will be kept as simple as possible; consequently the pulse curve will be considered as a type of distorted sine wave. The dicrotic notch will be neglected. In subsequent chapters more complicated analysis will be discussed.

Let the cardiovascular system be represented by a pump, the heart; an elastic volume container, the aorta; and a run off tube, the peripheral vessels giving rise to peripheral resistance. A model of this type is called in the German literature a "Windkessel", and is illustrated in Figure 7.1.

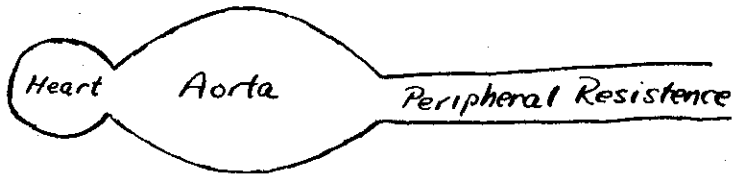


Figure 7.1. The Windkessel Model

a. The diastolic phase of the aortic pulse.

During this phase the inflow of blood from the heart to the aorta is zero. Assume that, 1) a linear relation exists in the aorta between volume and pressure, and 2) the system obeys Poiseuille's law.

Thus, with assumption 1, if $P = cV$, then

$$\frac{dP}{dV} = c, \tag{7.1}$$

where c is a constant, P is the pressure in the aorta, and V the volume of blood. Recall that Poiseuille-s law is

$$Q = \frac{P}{u} \text{ where } u = \frac{8l\eta}{\pi r^4}$$

and Q = volume flow, ml/time, u = resistance to flow, l = length of vessel, η = viscosity of blood, r = radius of vessel. Since, during diastole, the

volume flow is out of the aorta, and represents the rate of change of volume of the system, then

$$Q = -\frac{dV}{dt}$$

and Poiseuille's law can be written as

$$\frac{dV}{dt} = -\frac{P}{u} . \tag{7.2}$$

From (7.2), $dV = \frac{dP}{c}$. Substituting this value of dV into (7.1) gives

$$\frac{dP}{P} = \frac{c}{u}\, dt \tag{7.3}$$

Integrating:

$$\ln P = \frac{c}{u} t + C. \tag{7.4}$$

At $t = 0$, let $P = P_o$, then $c = \ln P_o$. Hence

$$\ln \frac{P}{P_o} = -\frac{c}{u} t$$

and

$$P = P_o e^{-\frac{c}{u} t} \tag{7.5}$$

Thus, from equation (7.5), with the assumptions made, it is seen that the pressure falls in the aorta during diastole in an exponential manner, with a time constant $T = \frac{u}{c}$.

b. The systolic phase of aortic pulse.

During this phase blood is pumped into the aorta from the heart. The volume change in the aorta is due to the rate of inflow plus the rate of outflow. Assume that the rate of outflow is given by Poiseuille's law:

$$\frac{dV}{dt} = \frac{P}{u}$$

as before, and that the rate of inflow, or some function of time, is i(t). Hence, the net change of volume per unit time in the aorta is

$$\frac{dV}{dt} = i(t) - \frac{P}{u} \tag{7.6}$$

Replacing dV with dP/c as before, (7.6) becomes:

$$\frac{dP}{dt} = c\left[i(t) - \frac{P}{u}\right]$$

or

$$\frac{dP}{dt} + \frac{c}{u}P = c\,i(t). \qquad (7.7)$$

In order to continue the analysis, it is now necessary to make some assumptions concerning the nature of the function i (t). Gross inspection of an aortic pulse curve would suggest that i (t) is perhaps a sine function. Hence, let i = A sin Bt. Since normally no regurgitation occurs, only the top portion of the sine curve need be considered, i.e., only values between t = 0 and $\frac{\pi}{B}$. (Figure 7.2).

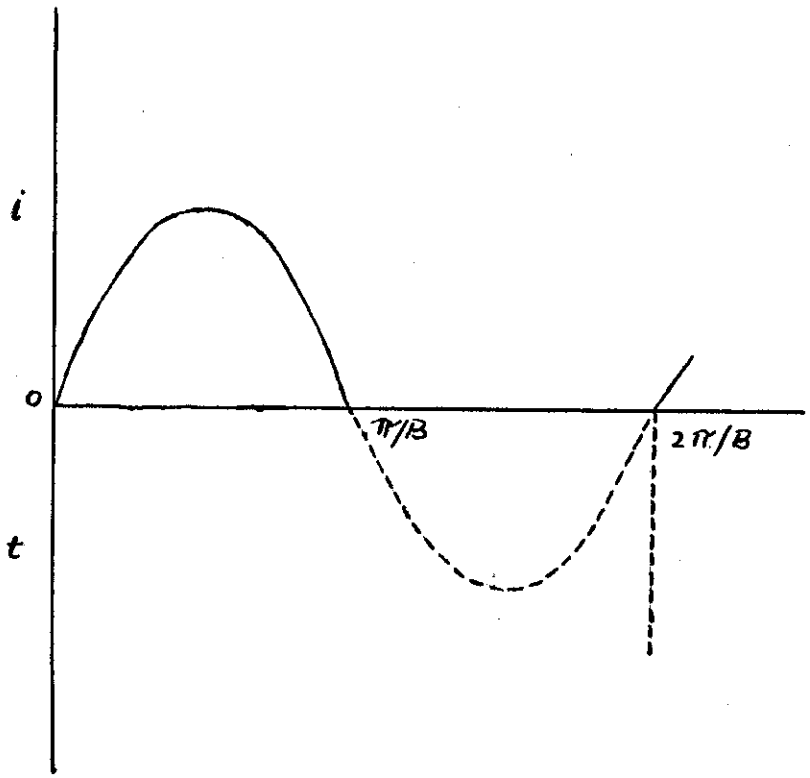


Figure 7.2. Assumed function i (t). Period = $\frac{2\pi}{B}$.

At any rate, substituting $i(t) = A \sin Bt$ into (7.7) gives

$$\frac{dP}{dt} + \frac{c}{u} P = cA \sin Bt \tag{7.8}$$

This equation is solved as follows:

Equation (7.8) is a linear 1^{st} order differential equation of the type

$$\frac{dy}{dx} + P(x)\, y = q(x) \tag{7.9}$$

where P (x) and q(x) are functions of x alone, not involving y. Such an equation is solved by multiplying it through by a suitable integrating factor. The general equation (7.9) has an integrating factor

$$e^{\int P\, dx} = e^{Px}.$$

Thus (7.9) is written

$$e^{Px} \frac{dy}{dx} + e^{Px} Py = e^{px} q(x). \tag{7.10}$$

Now, since $d(uV) = u(dV) + Vdu$, where u is set equal to y, $V = e^{Px}$, and

$$d(uV) = \frac{d}{dx} \left(y\, e^{Px} \right) = yPe^{Px} + e^{Px} \frac{dy}{dx},$$

equation (7.10) can be written as

$$\frac{d}{dx} \left(e^{Px}\, y \right) = q(x)\, e^{Px}. \tag{7.11}$$

Integrating (7.11) gives

$$ye^{Px} = \int q(x)\, e^{Px}\, dx + C$$

and

$$y = e^{-Px} \int q(x)\, e^{Px}\, dx + Ce^{-Px} \tag{7.12}$$

Consider now equation (7.8). In a similar fashion, this has an integrating factor

$$e^{\int \frac{c}{u} dt} = e^{\frac{c}{u} t}.$$

Hence, (7.8) becomes

$$e^{\frac{c}{u}t}\ \frac{dP}{dt} + \frac{c}{u}\,Pe^{\frac{c}{u}t} = cA \sin Bt\, e^{\frac{c}{u}t}$$

and

$$\frac{d}{dt}\left(Pe^{\frac{c}{u}t}\right) = cA \sin Bte^{\frac{c}{u}t} \quad . \tag{7.13}$$

Integrating (7.13),

$$Pe^{\frac{c}{u}t} = \int CA \sin Bt\, e^{\frac{c}{u}t}\ dt + D \tag{7.14}$$

where D is the constant of integration.

Hence

$$P = De^{-\frac{c}{u}t} + CA \int \sin Bt\, e^{\frac{c}{u}t} \quad . \tag{7.15}$$

From a table of integrals, it can be seen that the integral of (7.15) is of the form

$$\int e^{au} \sin nu\ du = \frac{e\,a\,u\ (a \sin nu - n \cos nu)}{a^2 + n^2} + C' \quad .$$

where $a = \frac{c}{u}$, $u = t$, and $n = B$.

Hence

$$\int \sin Bt\, e^{\frac{c}{u}t}\ dt = \frac{e^{\frac{c}{u}t}\left(\frac{c}{u} \sin Bt - B \cos Bt\right)}{\frac{c^2}{u^2} + B^2} + C' \quad .$$

Thus, from (7.14),

$$P = Ee^{-\frac{c}{u}t} + AC\ \frac{\frac{c}{u} \sin Bt - B \cos Bt}{\frac{c^2}{u^2} + B^2} \quad ,$$

where E is the new constant, a combination of C' and D. At $t = 0$, $P = P_o$ and

$$E = P_o + \frac{CAB}{\frac{c^2}{u^2} + B^2}$$

The complete solution is therefore

$$P = \left[P_o + \frac{CAB}{\frac{c^2}{u^2} + B^2}\right] e^{-\frac{c}{u}t} + \frac{AC\left[\frac{c}{u}\sin Bt - B\cos Bt\right]}{\frac{c^2}{u^2} + B^2} .$$

CHAPTER 8

TRANSPORT OF RADIOACTIVE SUBSTANCES IN A TWO COMPARTMENT SYSTEM.

Consider a two compartment system such as is illustrated in Figure 8.1. For purposes of discussion let compartment A represent blood plasma containing an amount P of K^{42}, and let B represent erythrocytes containing an amount Q of K^{42}.

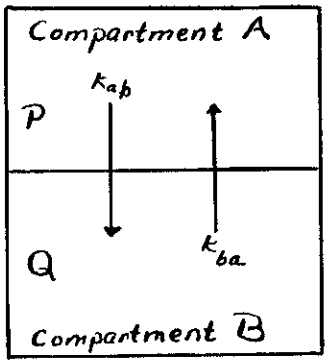


Figure 8.1. Plasma - red blood cell two compartment system.

If the assumption is made that the total amount of K^{42} in the system remains constant, then

$$P + Q = R, \tag{8.1}$$

where R is a constant. In addition, let the rate constant for K^{42} transport from A to B be k_{ab}, and from B to A, k_{ba}. For purposes of simplicity, assume that, although concentration differences may exist between compartments A and B, within each compartment the concentration is constant and no "inner" compartment diffusion gradients exist.

With these conditions, the rate of change of Q in compartment B is equal to the difference between the rates at which K^{42} is transported from A to B, $k_{ab}P$, and the rate at which it leaves, $k_{ba}Q$. Hence

$$\frac{dQ}{dt} = k_{ab}P - K_{ba}Q. \tag{8.2}$$

Since from equation (8.1), $P = R - Q$, equation (8.2) can be written

$$\frac{dQ}{dt} = k_{ab}R - (k_{ab} + k_{ba})\,Q$$

or

$$\frac{dQ}{dt} + (k_{ab} + k_{ba})\, Q = k_{ab} R \ .$$

The solution of this equation is easily seen to be as follows:

$$Q = \frac{k_{ab} R}{k_{ab} + k_{ba}} + Ce^{-(k_{ab} + k_{ba})t} \tag{8.3}$$

As a further condition, let the concentration of K^{43} in the red blood cells be zero at t = 0. Then from (8.3),

$$c = \frac{k_{ab} R}{k_{ab} + k_{ba}} \ ,$$

and (8.3) becomes

$$Q = \frac{k_{ab} R}{k_{ab} + k_{ba}} \left(1 - e^{-(k_{ab} + k_{ba})\, t}\right) \tag{8.4}$$

Since P = R − Q,

$$P = R - \frac{k_{ab} R}{k_{ab} + k_{ba}} \left(1 - e^{-(k_{ab} + k_{ba})\, t}\right)$$

$$= \frac{k_{ab} K}{k_{ab} + k_{ba}} \left(1 + \frac{k_{ab}}{k_{ba}}\, e^{-(k_{ab} + k_{ba})\, t}\right) \tag{8.5}$$

Note that as $t \to \infty$, the e term $\to 0$, so that

$$P_\infty = \frac{k_{ba} K}{k_{ab} + k_{ba}} \tag{8.6}$$

Thus equation (8.5) may be written as

$$P = P_\infty \left(1 + \frac{k_{ab}}{k_{ba}}\, e^{-(k_{ab} + k_{ba})\, t}\right),$$

or

$$\frac{P}{P_\infty} - 1 = \frac{k_{ab}}{k_{ba}}\, e^{-(k_{ab} + k_{ba})\, t}$$

and

$$\ln\left(\frac{P}{P_\infty} - 1\right) = -\left(k_{ab} + k_{ba}\right)t - \ln\left(\frac{k_{ba}}{k_{ab}}\right). \qquad (8.7)$$

P and P_∞ can be determined experimentally, P_∞ being that value of K^{42} in compartment A after a considerable length of time.

From analytical geometry, the equation of a straight line is $y = mx + c$, where m is the slope of the line, and c is the distance of intersection with the y axis from the origin. Thus if equation (8.7) were plotted, $\ln\left(\frac{P}{P_\infty} - 1\right)$ vs t (or $\left(\frac{P}{P_\infty} - 1\right)$ vs t on semi-log paper), then the slope of the line would be equal to $-(k_{ab} + k_{ba})$, and the y intercept $= -\ln\frac{k_{ba}}{k_{ab}}$.

Such a graph is shown in Figure 8.2, and from the slope and the intercept, the values of k_{ab} and k_{ba} may be determined.

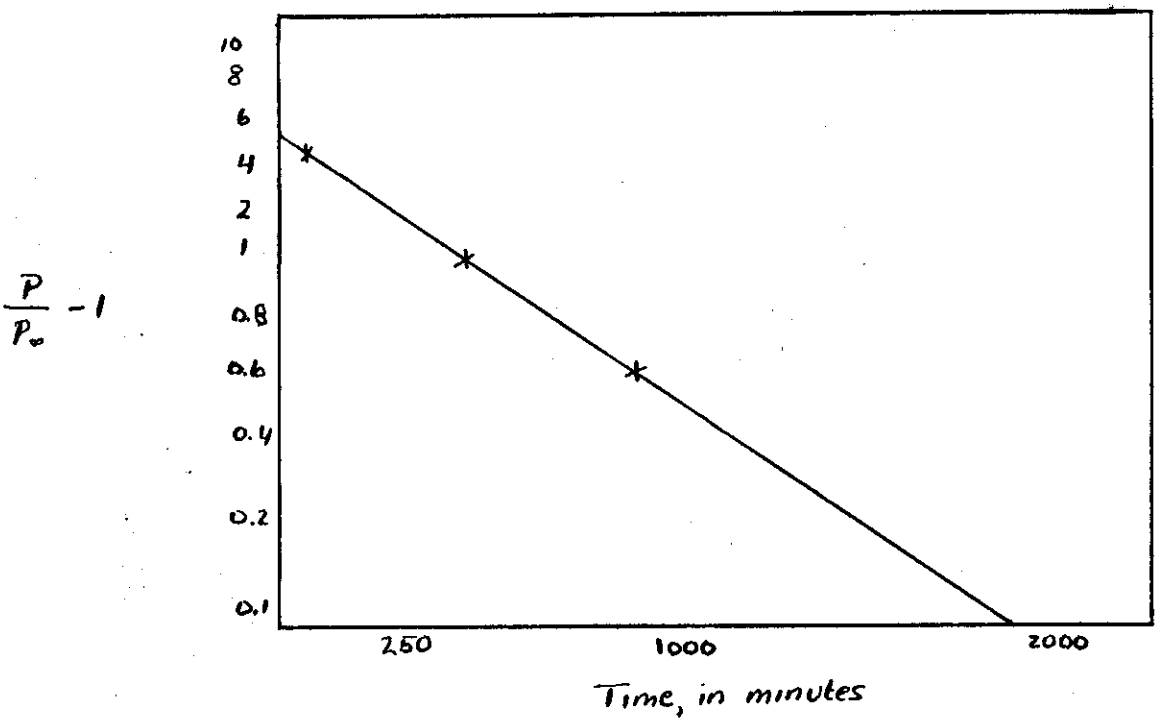


Figure 8.2. Semilogarithmic graph showing reduction of K^{42} from plasma with time: i.e., the uptake of K^{42} by red blood cells.

CHAPTER 9

TRANSPORT OF RADIOACTIVE SUBSTANCES IN A THREE COMPARTMENT SYSTEM.

Consider a three compartment system, such as the vascular system (compartment A), the interstitial space (compartment B), and the intercellular space (compartment C). Let there be a constant concentration, C_A, of a radioactive substance, such as glucose, in the vascular system, and let this substance be transferred across the capillary walls in both directions at the same rate, denoted by k_1. Also designate the total amount of the substance in compartment B by "B", and let its concentration in compartment B be

$$\frac{B}{V} = CB$$

where V is the volume of the compartment. Finally, let the substance be transferred, unidirectionally, from compartment B to compartment C at rate k_2. This might represent the utilization of glucose by the tissue cells. The system described is illustrated in Figure 9.1.

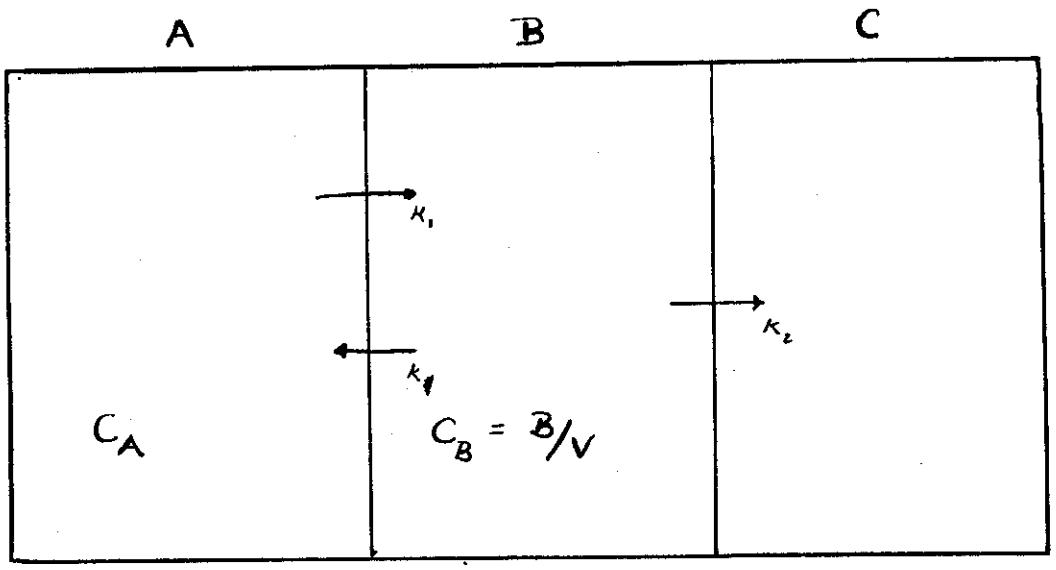


Figure 9.1. Transport of a substance in a three compartment system.

If the rate of change in the amount of substance in compartment B is directly proportional to the concentration of the substance in the blood, then

$$\frac{dB'}{dt} = k_1 C_A \, . \tag{9.1}$$

However, since there is also a movement of the substance from compartment B back to A, then

$$\frac{dB''}{dt} = - k_1 C_B \, , \tag{9.2}$$

where the movement is indicated as negative since the substance is decreasing in compartment B, and the movement is assumed to be directly proportional to the concentration in compartment B.

The net result of these two processes between compartments A and B is

$$\frac{dB'}{dt} + \frac{dB''}{dt} = \frac{dB'''}{dt} = k_1 C_A - k_1 C_B = k_1 (C_A - C_B) \tag{9.3}$$

If the radioactive substance is taken up by compartment C, at a rate k_2 and proportional to C_B, then

$$\frac{dB'''}{dt} = - k_2 C_B \, . \tag{9.4}$$

Therefore, the total net rate of change of the substance in compartment B is

$$\frac{dB}{dt} = k_1 (C_A - C_B) - k_2 C_B \, . \tag{9.5}$$

By definition, $C_B = B/V$, and $B = VC_B$, where V is the volume of compartment B and considered a constant. Hence equation (9.5) can be written

$$V \frac{dC_B}{dt} = k_1 (C_A - C_B) - k_2 C_B \, . \tag{9.6}$$

Equation (9.6) is solved as follows:

Rearranging terms and dividing through by V, (9.6) becomes:

$$\frac{dC_B}{dt} + \frac{(k_1 + k_2)\, C_B}{V} = \frac{k_1 C_A}{V} \tag{9.7}$$

Hence,

$$C_B = \frac{k_1 C_A}{k_1 + k_2} + Z \tag{9.8}$$

and

$$\frac{dC_B}{dt} = \frac{dZ}{dt} . \tag{9.9}$$

Substituting the values of C_B and $\frac{dC_B}{dt}$ from (9.8) and (9.9) into (9.7) gives

$$\frac{dZ}{dt} + \frac{(k_1 + k_2)}{V}\left(\frac{k_1 C_A}{k_1 + k_2} + Z\right) = \frac{k_1 C_A}{V} , \tag{9.10}$$

or

$$\frac{dZ}{dt} = -\frac{k_1 + k_2}{V} Z, \tag{9.11}$$

and

$$Z = A\, e^{-\frac{k_1 + k_2}{V} t} \tag{9.12}$$

where A is the constant of integration.

Substituting this value of Z into equation (9.8) gives

$$C_B = \frac{k_1 C_A}{k_1 + k_2} + A\, e^{-\frac{k_1 + k_2}{V} t} . \tag{9.13}$$

If the assumption is made that at t = 0, the amount of substance in compartment B = 0, then from (9.13)

$$A = -\frac{k_2}{k_1 + k_2} C_A \tag{9.14}$$

and (9.13) becomes

$$C_B = \frac{k_2}{k_1 + k_2} C_A - \frac{k_2}{k_1 + k_2} C_A e^{-\frac{k_1 + k_2}{V} t}$$

$$= \frac{k_2}{k_1 + k_2} C_A \left(1 - e^{-\frac{k_1 + k_2}{V} t} \right) \qquad (9.15)$$

At equilibrium, when $t = \infty$, then

$$\frac{C_B}{C_A} = \frac{k_2}{k_1 + k_2} \cdot \qquad (9.16)$$

CHAPTER 10

NEUROPHYSIOLOGY: CONCENTRATION OF ANESTHETIC IN BRAIN TISSUE.

The effects of an anesthetic on brain tissue is dependent upon the time course of the concentration of the anesthetic agent. Such a time course is determined as follows.

Assume that

a. The arterial concentration and alveolar concentration of the agent remain constant.
b. Complete equilibrium is reached between the brain tissue and the blood, and that the partition coefficient, i.e., the solubility, for brain tissue and blood is the same. For ether, the brain-blood partition coefficient is 1 : 1.4.

Denote the agent concentration in the brain and in the venous blood by c_B and c_V respectively. Then

$$c_B = c_V \tag{10.1}$$

The amount of agent in the arterial blood is c_a molecules/liter, and the arterial flow is F liters/minute. Hence Fc_a is the amount of agent brought to the brain per minute. Likewise, let Fc_V = amount leaving brain/minute. Hence, the rate of uptake of agent by the brain is

$$\frac{dQ}{dt} = Fc_a - Fc_V = F\,(c_a - c_V)\ , \tag{10.2}$$

where Q is the amount of agent in the brain. If v = volume of brain, then $Q = c_B v$. Thus (10.2) becomes

$$\frac{dc_B}{dt} = \frac{F}{v}\,(c_a - c_v), \tag{10.3}$$

and since $c_v = c_B$,

$$\frac{dc_B}{dt} = -\frac{F}{v}\,(c_B - c_a) \tag{10.4}$$

Assume that F, c_a, and v are constant. Then, separating the variables gives

$$\frac{dc_B}{c_B - c_a} = -\frac{F}{v}\,dt \tag{10.5}$$

Integrating [from tables, $\int \frac{dx}{a + b_x} = \frac{1}{b}\log\,(a + b_x)$]

$$\ln\,(c_a - c_B) = -\frac{F}{v}t + C \tag{10.6}$$

If at $t = 0$, $c_B = 0$, $C = \ln C_a$, and (10.6) is

$$\ln\,(c_a - c_B) - \ln c_a = -\frac{F}{v}t\,, \tag{10,7}$$

or

$$\ln \frac{c_a - c_B}{c_a} = -\frac{Ft}{v}$$

and

$$\frac{c_a - c_B}{c_a} = e^{-\frac{Ft}{v}}$$

and

$$c_B = c_a\,(1 - e^{-\frac{Ft}{v}}) \tag{10.8}$$

Thus, the concentration of anesthetic in the brain rises as a single exponential function.

CHAPTER 11

QUANTITATIVE ASPECTS OF MUSCULAR EXERCISE: INTRODUCTION.

In this chapter we will begin consideration of the problem of muscular exercise.

In the resting state, the human body consumes about 250 cc. of oxygen per minute. The maximum possible oxygen uptake for a trained athlete in a steady state of exercise seems to be about 4 liters per minute, or a 16-fold increase over the resting state. (non-athletic subjects average less than three liters per minute). At any steady state level, the rate of oxygen consumption is proportional to the rate of exercise. The relationship is seen in Figure 11.1 where oxygen consumption is plotted as a function of the steady state rate of running. Values of oxygen consumption above the maximum of 4 liters/minute are extrapolated.

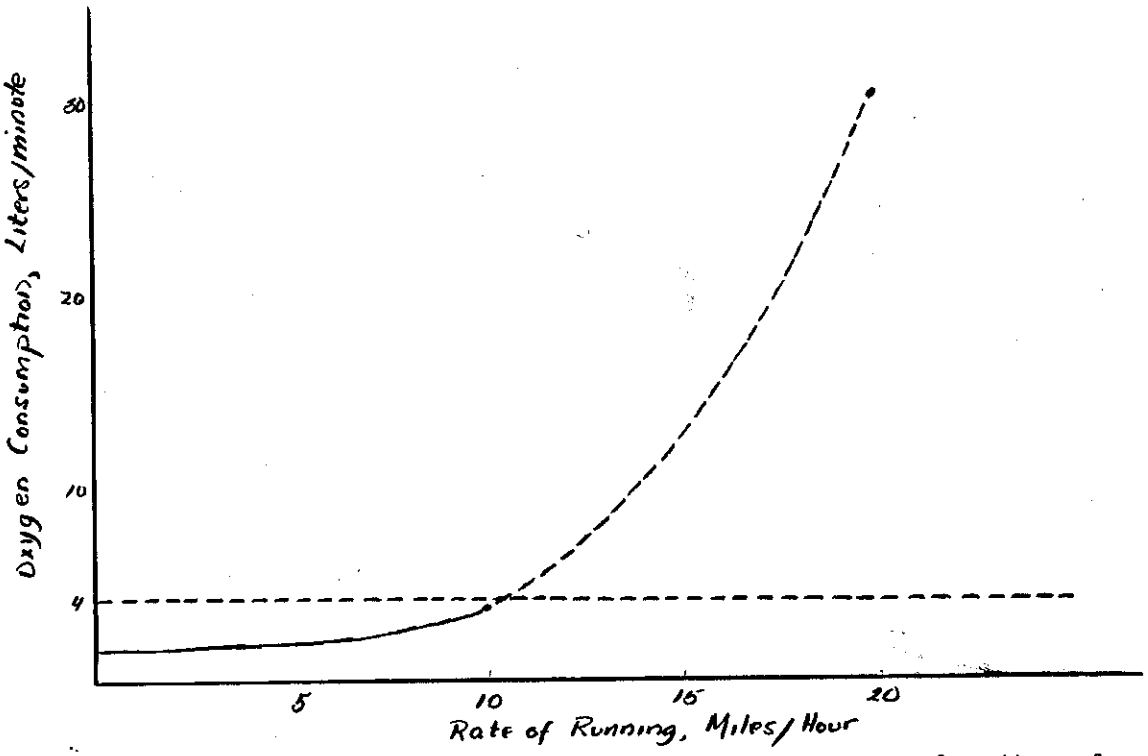


Figure 11.1. Rate of oxygen consumption as a function of rate of exercise.

From Figure 11.1 it is apparent that the maximum rate of oxygen consumption is achieved at a rate of approximately 10 miles per hour, and running at speeds faster than this will prohibit the obtaining of a steady state condition, and the rate at which oxygen debt occurs is greater than the rate at which energy is being used by the body.

Experimentally, oxygen debt can be measured as the amount of oxygen above the basal level which is consumed following a period of exercise. For example, from Figure 11.2 let period 1 represent the period of rest before exercise, 2 the period from the onset of a steady rate of exercise to the obtainment of a steady rate of oxygen consumption, 3 the period of the steady state, and 4 the period of excess oxygen consumption after cessation of exercise. The amount of oxygen debt is then the area under the curve of period 4.

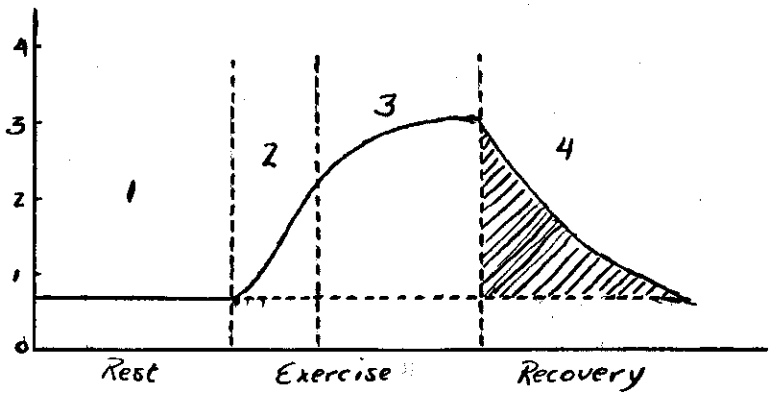


Figure 11.2. Oxygen consumption before, during, and after a period of exercise.

The maximum amount of oxygen debt that has been recorded is about 18 liters. If the 100 yard dash represents the maximum exercise possible, then it can be easily calculated that the limitation of the velocity of the dash is not due to oxygen debt. For example, the velocity for the dash is about 22.6 miles per hour, and from Figure 11.1 this would require at the steady state condition, an oxygen requirement of about 30 liters per minute. Since a 100 yard dash can be run in about 9 seconds, it would require about 4.5 liters of oxygen. During this period about 0.5 liters of oxygen can be consumed, leaving a debt of 4 liters, far below the maximum possible.

In muscular exercise, carbohydrate is used almost exclusively as an energy source, and it is of interest to consider when this becomes a limiting factor. Assume that in a 70 kg. man there are 28 kg. of muscle, and 2.1 kg. of liver. Also assume that muscle contains 1.8% glycogen, and liver 10%. Then the total glycogen content in a 70 kg. man would be 710 grams. If a runner is engaged in a marathon, at a maximum steady state speed of about 10 miles/hour, consuming 4 liters of oxygen per minute, and if the 710 grams of glycogen is the sole source of fuel, then it would last for 2.2 hours. This is slightly less than the record of 2.6 hours for the standard 26 mile marathon run, and it is perhaps significant that runners supplement their glycogen supply with candy or sweetened tea during the course of the run. The specific calculations resulting in the 2.2 hour figure are as follows. The reaction for the breakdown of glycogen is

$$C_6H_{12}O_6 + 6\ O_2 \rightleftharpoons 6\ CO_2 + 6\ H_2O$$

Since the molecular weight of the sugar is 180, and of 6 O_2 is 192, and since there are 710 grams of glycogen (sugar) available, then

$$\frac{180}{710} = \frac{192}{x}\ ,\quad x = 756 \text{ grams}$$

of oxygen needed to oxidize the available carbohydrate. Also, since at standard conditions, 32 grams of oxygen occupy 22.4 liters of space, 756 grams of oxygen would occupy 525 liters of space. Hence, if 4 liters of oxygen are burned per minute, then 525 liters would be burned in 131.3 minutes, or 2.19 hours. In other words, at the maximum steady state rate of oxygen consumption possible, all the available carbohydrate would be consumed in approximately 2.2 hours.

Another facet of muscular exercise is the problem of the dissipation of heat produced by the exertion. In performing external work, muscles are only about 20% efficient; i.e., about 80% of the energy used in exercise is given off as heat. About 75% of this heat is given off from the skin, the remaining 25% from the lungs (warming inspired air). It is of interest to cal-

culate the cutaneous blood flow necessary for the dissipation of this heat.

Let the steady state uptake of oxygen in exercise be 4 liters per minute, and let, in the burning of carbohydrate, one liter of oxygen evolve 5 large calories of heat. Then the amount of heat produced by the body referrable to the skin (75%) is

$$H = 0.75 \times 5 \times 4 \times 0.8 = 12 \text{ k cal./min.}$$

The 0.8 in the calculation refers to the 80% of fuel consumption given off as heat.

This amount of heat, if dissipated by the skin, would also be equal to the fall in temperature of cutaneous blood, $\Delta T°C$, times the blood flow to the skin, F_s in liters/minute, times the specific heat of blood, 0.85, or

$$F_s \times \Delta T°C \times 0.85.$$

If the body temperature is maintained at 37° C, and if the normal mean skin temperature is taken as 30° C, and if it is assumed that the fall in temperature of blood coursing through the skin averages between these values, then

$$12 = F_s \times \frac{37 - 30}{2} \times 0.85$$

and

$$F_s \cong 4 \text{ liters per minute.}$$

If the cardiac output during such a period of exercise is 30 liters per minute, then cutaneous blood flow would be 13% of the total.

CHAPTER 12

QUANTITATIVE ASPECTS OF MUSCULAR EXERCISE, CONTINUED.

Much of the material of the preceding chapter can be refined and developed as follows.

Assume that during exercise the oxygen debt in proportional to the work done. If oxygen debt is denoted by x, and the work done by W, then

$$x' = \alpha W \tag{12.1}$$

where α is the constant of proportionality. If now equation (12.1) is differentiated with respect to time,

$$\frac{\alpha x'}{dt} = \alpha \frac{dW}{dt}, \tag{12.2}$$

which states that the change in oxygen debt per unit time is proportional to the change of work per unit of time.

On the other hand, if the assumption is made that the oxygen debt is dependent upon the amount of oxygen taken up by the lungs, i.e., the oxygen supply, then

$$\frac{dx''}{dt} = -\frac{dO}{dt} \tag{12.3}$$

where O indicates the amount of oxygen uptake, and the minus sign indicates that as the oxygen consumption increases, the oxygen debt decreases.

It is obvious that the rate of change of oxygen debt is (12.2) – (12.3), or

$$\frac{dx}{dt} = \alpha \frac{dW}{dt} - \frac{dO}{dt} \tag{12.4}$$

If it is further assumed that the rate of change of oxygen uptake is proportional to the oxygen debt existing at any instant, then

$$\frac{dO}{dt} = k_x \tag{12.5}$$

and (12.4) becomes

$$\frac{dx}{dt} = \alpha \frac{dW}{dt} - k_x \tag{12.6}$$

or

$$\frac{1}{k}\frac{dx}{dt} + x = \frac{\alpha}{k}\frac{dW}{dt}. \tag{12.7}$$

Letting $\frac{1}{k} = \tau$, and $\frac{dW}{dt} = P(t)$, then (12.8) is

$$\tau\dot{x} + x = \frac{\alpha}{k}P(t) \tag{12.8}$$

Consider now the case where $P(t) = 0$, as for example at the end of a period of exercise. Then (12.8) is

$$\tau\dot{x} + x = 0 \tag{12.9}$$

The solution of (12.9) is as follows:
Write (12.9) as

$$\frac{dx}{dt} = -\frac{x}{\tau}$$

and

$$\frac{dx}{x} = -\frac{1}{\tau}dt.$$

Integrating:

$$\ln x = -\frac{1}{\tau} + \ln C$$

and

$$\ln\left(\frac{x}{c}\right) = -\frac{t}{\tau}$$

or

$$x = C\,e^{-\frac{t}{\tau}} \tag{12.10}$$

At $t = 0$, $C = x_o$, i.e., the oxygen debt at $t = 0$; hence (12.10) is

$$x = x_o e^{-\frac{t}{\tau}} \tag{12.11}$$

Equation (12.11) would indicate that the oxygen debt falls to zero after cessation of exercise in an exponential manner. Since oxygen debt cannot be measured directly, the problem is to verify the equation. This is done

through the following procedure. Since from equation (12.5),

$$x = \frac{1}{k}\frac{dO}{dt},$$

substituting this value of x into (12.11) gives

$$\frac{dO}{dt} = k\,x_o\,e^{-\frac{t}{\tau}} \qquad (12.12)$$

In practice, the rate of excess oxygen uptake, $\frac{dO}{dt}$, can be measured. Experimentation shows, that as would be dictated by (12.12), this rate decreased in a manner suggesting an exponential function, and is shown in Figure 12.1.

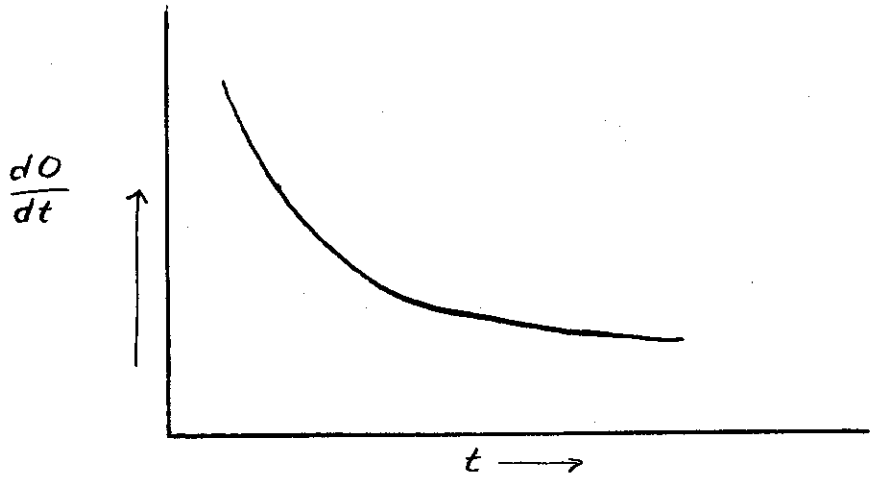


Figure 12.1. Decrease of dO/dt with time.

The area under the curve of figure 12.1 represents the value for x_o, the area being the integral of equation (12.12). If the end of exercise is taken as t = 0, then

$$\int_0^\infty k x_o\, e^{-\frac{t}{\tau}} = -\tau k x_o\, e^{-\frac{t}{\tau}}\Big|_0^\infty$$

$$= -x_o\, e^{-\frac{t}{\tau}}\Big|_0^\infty = x_o\ .$$

Hence $\tau = 1/k$. Here, x_o is the oxygen debt at the instant exercise ended.

CHAPTER 14

NEUROPHYSIOLOGY: HOORWEG'S EQUATION FOR EXCITATION.

One of the earliest attempts to formulate the phenomena of excitation in mathematical terms was that of Hoorweg. It is presented here so that the student might be familiar with the reasoning behind the effort. Basically, the theory accounts for two properties of excitation:

1. the strength-duration curve, which is represented approximately by a hyperbola, and
2. the phenomena of accomodation; if the stimulating current increases sufficiently slowly, it may fail to cause excitation even at values greater than threshold.

Hoorweg assumed the following: that a nerve impulse is released only when the stimulating current causes the release of an amount of excitatory substance, ϵ, to or exceeding a critical level, ϵ_0. He further assumed that the rate of release of ϵ was some function of the stimulating current, i (t), times an exponential term:

$$\frac{d\epsilon}{dt} = i\,(t)\, e^{-\beta t} . \qquad (14.1)$$

Thus

$$\epsilon = \int_0^t i\,(t)\, e^{-\beta t}\, dt \qquad (14.2)$$

That equation (14.2) accounts for the hyperbolic nature of the strength-duration curve is seen as follows. In this relationship i (t) is a <u>constant</u> current of threshold strength, suddenly applied at t = 0. Letting i (t) = i = a constant value, then (14.2) becomes:

$$\epsilon = i \int_0^t e^{-\beta t}\, dt = -\frac{i}{\beta} e^{-\beta t} \Big|_0^t$$

$$= -\left[\frac{i}{\beta} e^{-\beta t} - \frac{i}{\beta} \right] = \frac{i}{\beta} \left(1 - e^{-\beta t} \right) \qquad (14.3)$$

Since here $\epsilon = \epsilon_o$, solving (14.3) for i gives

$$i = \frac{\beta \epsilon_o}{1 - e^{-\beta t}} \tag{14.4}$$

Equation (14.4), however, is not clearly that of a hyperbola, so the following transformations are made. Writing (14.4) as

$$e^{\beta t} = \frac{i}{i - \beta \epsilon_o} \quad , \tag{14.5}$$

and since

$$e^{\beta t} = 1 + \frac{\beta t}{1!} + \frac{\beta^2 t^2}{2!} + \frac{\beta^3 t^3}{3!} \quad ,$$

neglecting the higher terms, (14.5) is

$$1 + \beta t = \frac{i}{i - \beta \epsilon_o} \; . \tag{14.6}$$

Multiplying (14.6) through by $i - \beta \epsilon_o$ gives

$$i = i - \beta \epsilon_o + i \beta t - \beta \epsilon_o - \beta t$$

or

$$i = \frac{\epsilon_o}{t} + \beta \epsilon_o \quad , \tag{14.7}$$

which clearly represents a hyperbola.

That equation (14.2) accounts for the second property of excitation, that slowly rising currents fail to excite a nerve is seen in the following:

Let a linearly rising current by $i = \lambda t$, where λ is a positive constant. Then (14.2) is

$$\epsilon = \lambda \int_0^t t \, e^{-\beta t} \, dt \; . \tag{14.8}$$

From tables of integrals,

$$\int x \, e^{-ax} \, dx = - \frac{e^{-ax}}{a^2} (ax - 1),$$

(14.8) is seen to be

$$\epsilon = \frac{\lambda}{\beta}\left[\frac{1}{\beta} - \left(t + \frac{1}{\beta}\right) e^{-\beta t}\right] . \qquad (14.9)$$

From (14.9) it is seen that ϵ tends asymptotically to λ/β^2. Hence if $\epsilon_0 > \lambda/\beta^2$, then ϵ will never reach the value ϵ_0, and the nerve will not be excited. Thus Hoorweg's equation accounts for the two stated properties of excitation.

CHAPTER 15

QUALITATIVE DESCRIPTION OF A SINGLE MUSCLE TWITCH

The purpose of this chapter is to describe some of the events which occur when skeletal muscle is stimulated to contract, producing what is known as a twitch. Many different kinds of events occur, and these will be discussed under various headings.

A. Electrical Events

The electrical events following stimulation of a muscle and related to the sarcolemma proceed the mechanical response and are similar in nature to the electrical events observed from an activated nerve fiber. Figure 5.1 illustrates the membrane potential changes.

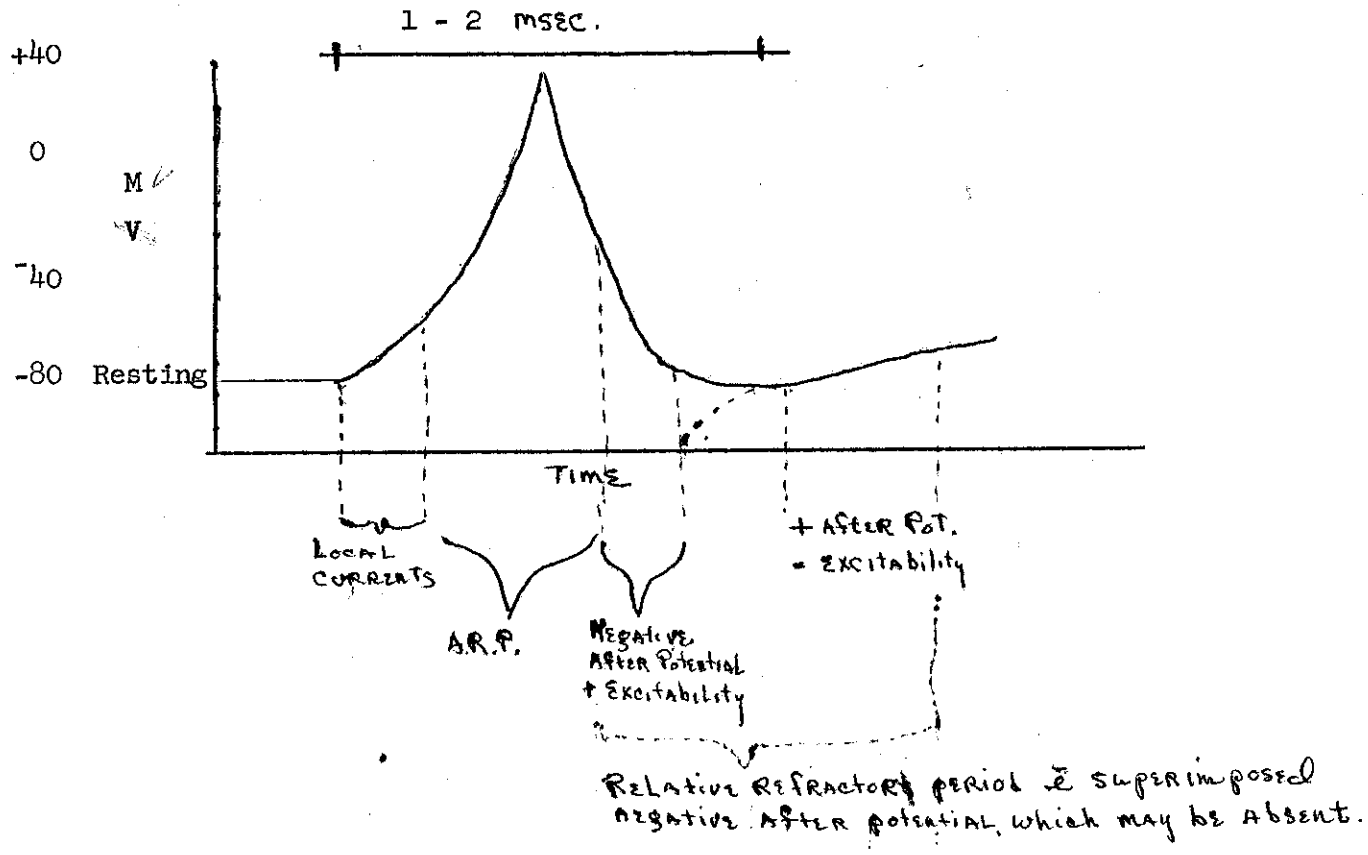


Figure 15.1 - Electrical Charges of Muscle Membrane; The Action Potential

The first part of the action potential represents slowly rising currents - electrotonic potentials - which precede the impulse, followed by the sharp rising spike potential, which signifies excitation of the muscle contractile components. Normally, a spike potential is always associated with a muscle contraction, and the contraction wave of muscle follows in time. Figure 15.1 is self explanatory.

B. The Mechanical Events

A typical mammalian action potential, minus the after potentials, may last 1 to 2 msec. The first observed mechanical response occurs about 2 msec. after the completion of the local currents and the beginning of the rise of the spikes. The beginning of the rise of the spike has been regarded as the beginning of the excitation processes in the muscle. Therefore, between the time and the first mechanical response there are 2 msec. of no mechanical activity, and is termed the latency period of muscular contraction; that time from the first excitation of muscle to the first mechanical response. The membrane may be completely repolarized during this time and the action potential, except for the long drawn out positive after potential (50 - 150 msec.), completed.

The first detectable mechanical change, is the slight lengthening of the muscle; as though to all appearances the muscle relaxes slightly more than in the resting state. This lengthening reaction is termed the latency relaxation of muscle. Latency relaxation is followed within a few tenths of a msec. by shortening of the muscle, or by the contraction in which the muscle develops tension. The muscle will continue to develop tension or continue to shorten for approximately 30 to 40 msec., when the tension and shortening reach a maximum. This is followed by relaxation or lengthening of the muscle, complete (to the resting base line) in about 60 to 70 msec. The relationships are seen in Figure 15.2.

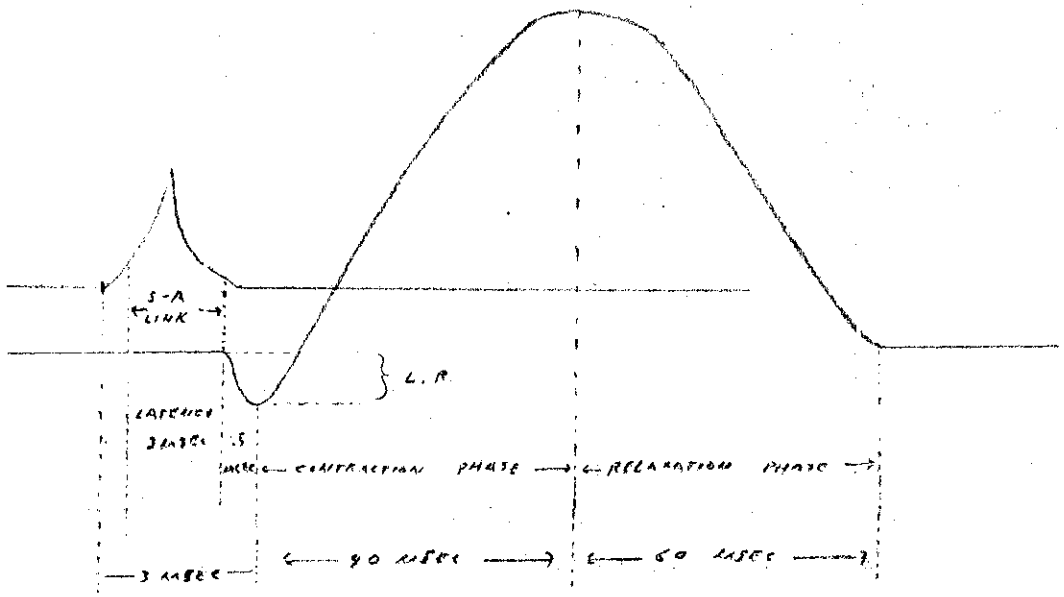


Figure 15.2 - Electrical and Mechanical Relationships of a Muscle Twitch

Notice that the relaxation phase of the contraction cycle is longer than the contraction phase. It is felt by many that the depolarization of the membrane initiates or activates in some way, the contractile mechanism of the muscle. Thus, the beginning of the spike potential to the beginning of the mechanical response is said to be the spike - activation link -, roughly correlating with the latency period. During this time, reactions initiated in the membranes are believed to be transferred in some manner to the contractile units causing their activation.

C. Ionic Events

Associated with the membrane events are ion or electrolyte charges across the membrane and in the muscle proper. These are as follows:

With the rise of the spike potential there is simultaneously a movement inward across the membrane of the Na ions, and as the spike wanes, K^+ ions flow across the membrane out of the tissue. There is also considerable evidence that Ca^{++} ions are released from the membranes during the

spike, and these Ca^{++} ions move into the cytoplasm of the tissue, and also out across the membrane to the extracellular fluid. With the wane of the spike, at the close of the action potential, the Na^{+} ions are again slowly extruded and K^{+} ions again reenter the cell, and the amount of free calcium ion in the cytoplasm decreases, apparently becoming bound in the membrane again. These are the main electrolyte changes which occur during an action potential, and are shown in Figure 5.3.

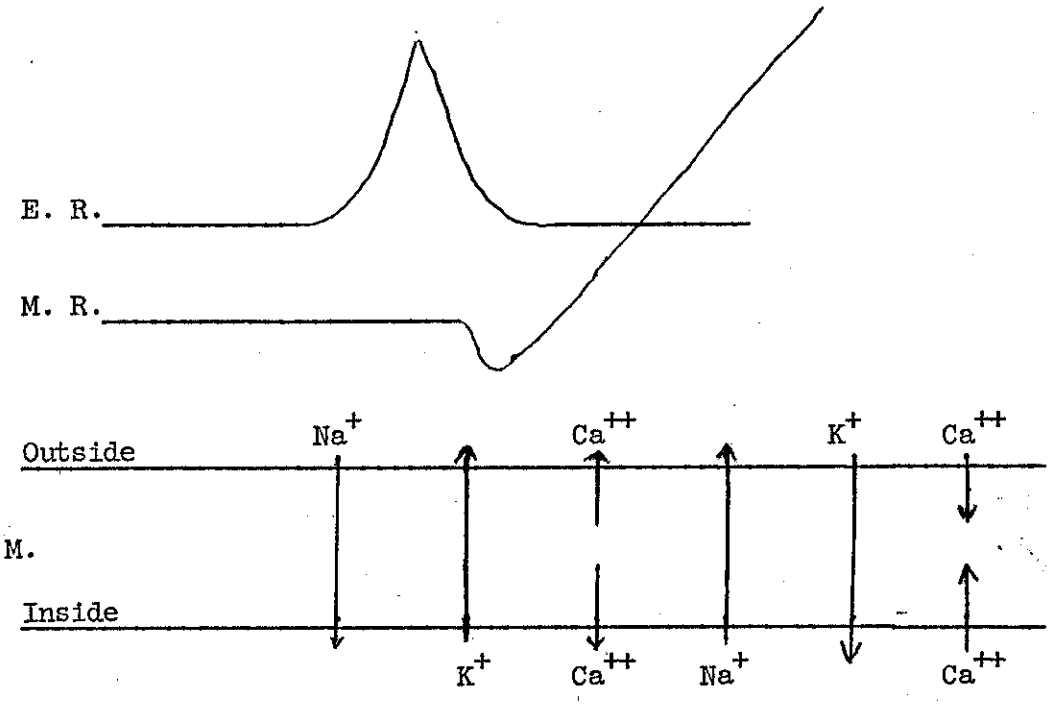


Figure 5.3 - Ionic Changes During a Muscle Twitch

D. Oxygen Consumption (Metabolism) and Heat Changes

Before discussing the oxygen consumption during a twitch, it is well to very briefly and grossly describe the main metabolic pathways in muscle which release the energy ultimately used for contraction. The details of these pathways, you have learned in biochemistry.

The energy for contraction is ultimately derived from the oxidation of carbohydrate, which becomes converted to CO_2 and H_2O. Thus, a glucose molecule contains in its organization a certain amount of energy which may be released as the molecule is broken down to CO_2 and H_2O. The breaking up of glucose is accomplished by removing electrons (oxidation) from the molecule.

$$C_6H_{12}O_6 \rightarrow C^{++++} + H^{+} + \text{Smaller Units} + \text{Energy} + \text{Electrons}$$

Oxygen is used in the processes to combine with the liberated electrons: $O \rightarrow O^{=}$. Without the presence of oxygen, the metabolic systems would soon become saturated with electrons and the processes would stop. The reduced oxygen $O^{=}$, combines with the oxidized C^{++++} and H^{+} forming CO_2 and H_2O. Thus:

$$\underset{\text{(Bound Energy)}}{C_6H_{12}O_6} + 6O_2 \rightarrow 6CO_2 + 6H_2O + \text{Freed Energy}$$

The reaction goes to completion in two main steps. The first step involves the initial break up of glucose into three carbon units, releasing some energy, by a series of reactions which do not immediately require the presence of oxygen. This series of reactions appropriately has been termed anaerobic, in which glucose (or glycogen) is converted to pyruvic or lactic acid, 3 carbon units. This is also called glycolysis. The second main step involves, or requires, a more close relationship with oxygen, and will not proceed in its absence. In this series of reactions, the 3 carbon units are broken down to CO_2 and H_2O with the liberation of large amounts of energy. The series of reactions are called aerobic metabolism, and follows the anaerobic breakdown of glucose to lactic acid or pyruvic acid. If oxygen is present so that aerobic metabolism may proceed, pyruvic acid alone is formed. If oxygen is not present, then the pyruvic acid is converted into lactic acid. The overall reactions can be diagramed as follows:

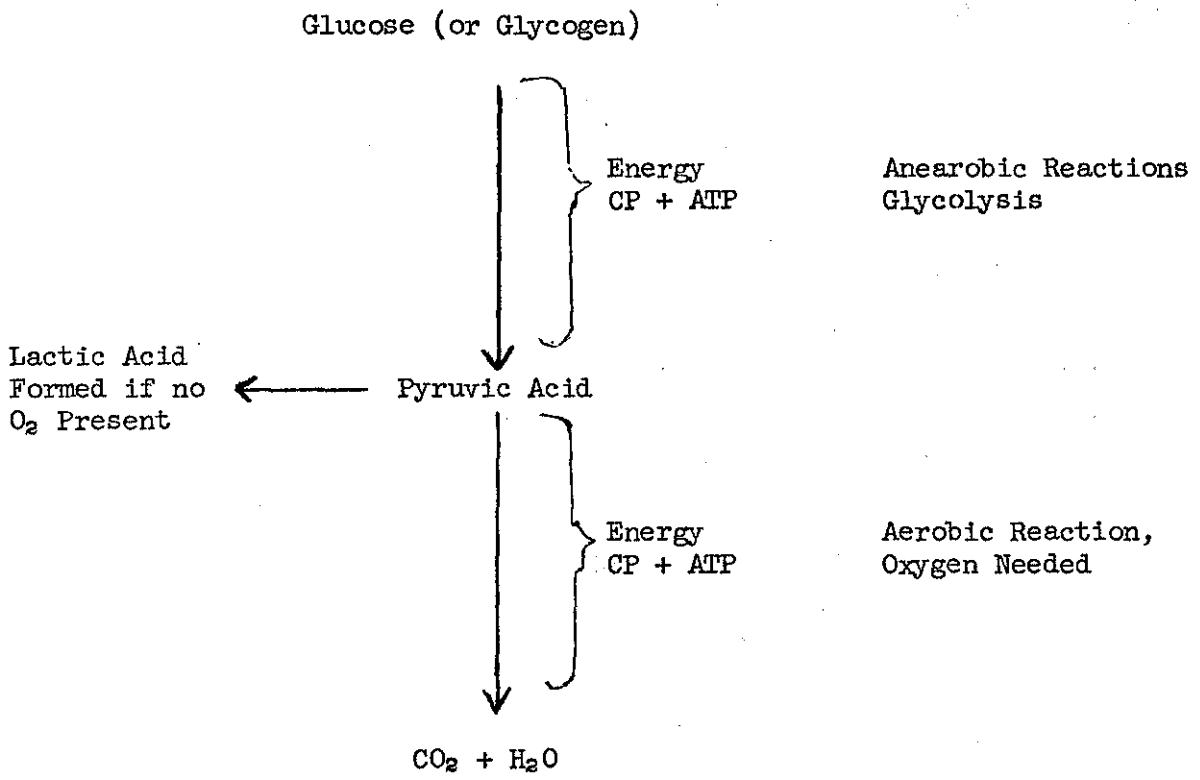


Figure 15.4 - General Metabolism of Muscle

In muscle, the energy given off in these reactions can partially (5 to 20% efficient) be used in the contractile processes for shortening and work. Since these reactions are of low efficiency, a large amount of energy is given off as heat, which cannot be utilized directly in the contractile mechanism. A large portion of the energy given off by the breakdown of glucose is stored in potential form in the organization of the molecules, creatine phosphate and adenosine-triphosphate. These cycles therefore hold, as it were, the energy from metabolism in their chemical organization until it is released for, or during, contraction. The largest

reserve of energy is in CP. ATP is more intimately associated with the contractile process and its energy is first used as the compound is broken down during the contractile processes.

The ATP is in dynamic equilibrium with CP, and as its ~~ions are~~ concentration is lowered, CP is used in that it builds ~~it~~ ATP back up to normal levels:

$$CP \rightleftarrows ATP.$$

With this very simple scheme of muscle metabolism in mind, the following changes during contraction may be better appreciated.

In the resting muscle, there is a constant consumption of oxygen and a constant basal heat production. This is because there is a continual breakdown and resynthesis of the muscle structure, and an inherent instability of ATP and CP.

No added oxygen consumption occurs during the contraction of the muscle (still a single twitch), but only after the mechanical response has been completed. Then it remains above the resting level for a prolonged time, only gradually returning to normal. The heat changes are as follows: The first heat increase over basal level occurs during the latter half of the latent period, before any shortening of the muscle occurs. This is called the activation heat and it is substantial in amount. It blends with another heat quantity produced as the muscle shortens, but this heat production occurs at a slow rate, and is called the shortening heat. Activation heat plus shortening heat together are called the initial heat production of a muscle contraction. After the twitch or mechanical response has occurred, there is a long period of heat production coinciding with the increased oxygen consumption. This is called the recovery heat. Quantitatively, the activation heat is about half the maximum shortening heat, and the initial heat is about equal to the recovery heat. The recovery heat lasts some 600 times as long as the initial heat.

These changes are diagramed in Figure 5.5.

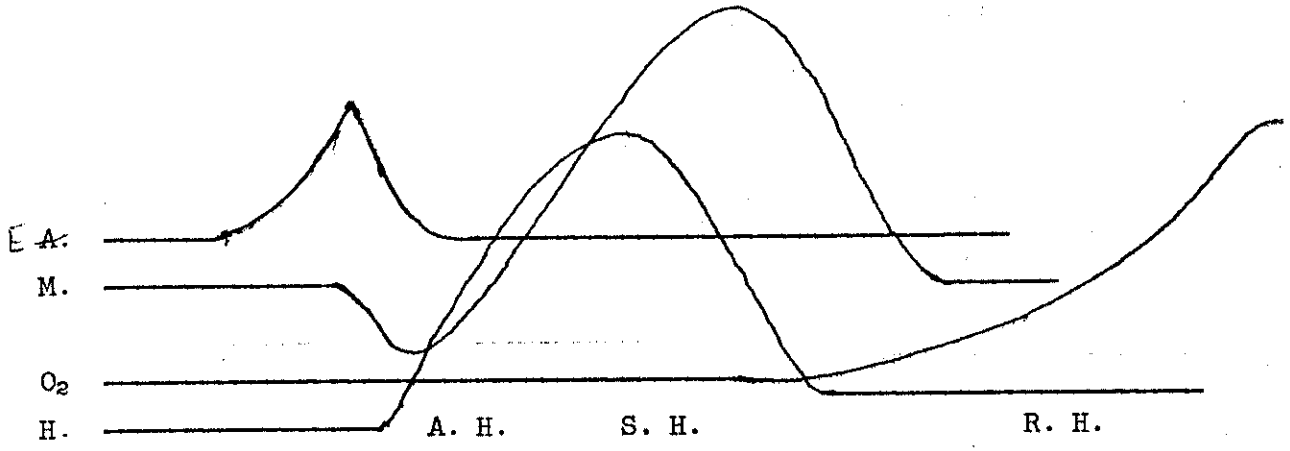


Figure 15.5 - Oxygen Consumption and Heat Production During a Single Twitch

E. pH Changes

The last parameter to discuss in connection with a muscle contraction is that of pH.

The resting pH of muscle is thought to be around 6.9. At the onset of contraction, there occurs a slight increase in alkalinity, coinciding with the onset of recorded tension. Following this, there is a slight acid shift during contraction which gradually reverts to a marked alkaline phase. These changes have been attributed to the following. The first alkaline phase is believed to result from the formation of actomyosin from myosin and actin. The second acid phase is believed to be due to the splitting of ATP to ADP. The third alkaline phase is attributed to the dephosphorylation of CP. These changes are shown in Figure 15.6.

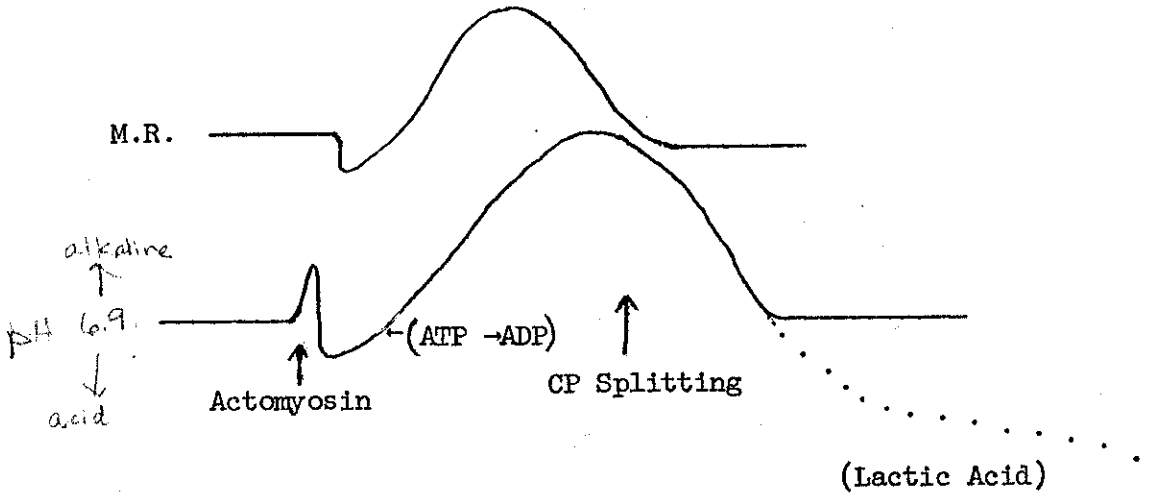


Figure 15.6 - pH Changes During a Muscle Twitch

To this diagram should be added (if contract) a fall in pH to the acid side (if the muscle is repeatedly stimulated to contract) due to lactic acid formation.

In summing then, the following events occur during a single muscle twitch.

As the impulse travels down the motor nerve, it reaches the motor end plate region. By means of acetylcholine, an end-plate potential is produced. The potential spreads to the surrounding membrane eliciting a propagated spike over the surface of the muscle fiber. With the rapid rise in spike potential, Na^{+} enters the fiber, and as the spike wanes, K^{+} leaves the cell and Ca^{++} is freed from the membrane to the interior and exterior. After the spike, the muscle begins to lengthen. Heat production suddenly increases, and the muscle pH becomes slightly acidic. Actomyosin is formed, and a rise in heat is caused by the splitting of ATP. This is accompanied

by a further increase in acidity. Shortening of the muscle begins, with further heat liberation. Na^+ is extruded from the cells, and K^+ begins to reenter. The pH of the fiber becomes markedly alkaline, due to CP breakdown in replenishing the ATP. Ca^{++} is rebound in the membrane and contraction gives way to relaxation; the initial heat declining into the recovery heat. Oxygen consumption begins to increase, as metabolism is stimulated, to replenish the metabolised CP. As CP is restored, the pH returns to normal. The mechanical response is over, but the oxygen consumption and heat production remains high until the energy reserves are fully replenished.

CHAPTER 16

QUALITATIVE DESCRIPTION OF CERTAIN OTHER ASPECTS OF MUSCLE BEHAVIOR

A qualitative description of certain aspects of muscle behavior other than the single twitch is useful before quantitative descriptions are attempted.

A. Length-tension Diagram

One important property is the relationship between length of a muscle and the tension developed upon stimulation. Recall that changing the length of a muscle influences the work which the muscle will perform, or the tension which the muscle will develop. The distinction which is placed on the words work and tension, as applied to muscle, is briefly as follows:

If a muscle is allowed to shorten with an attached load, as it is stimulated, then the load is lifted over a certain distance, depending upon the degree of shortening, and work is accomplished. Such a contraction is termed an isotonic contraction since, after the load is first lifted, the tension on the muscle remains the same, as the weight remains the same. But if the ends of the muscle are held rigid and not allowed to shorten when stimulated, then tension in the muscle increases to a maximum and then falls off. Since in this instance the tension on the muscle varies during the contraction cycle, and since here the length remains more or less fixed, this type of contraction is called isometric.

With regard to the work output or tension development and length of the muscle fiber, the relationships are generally the same, and are diagramed in Figure 16.1.

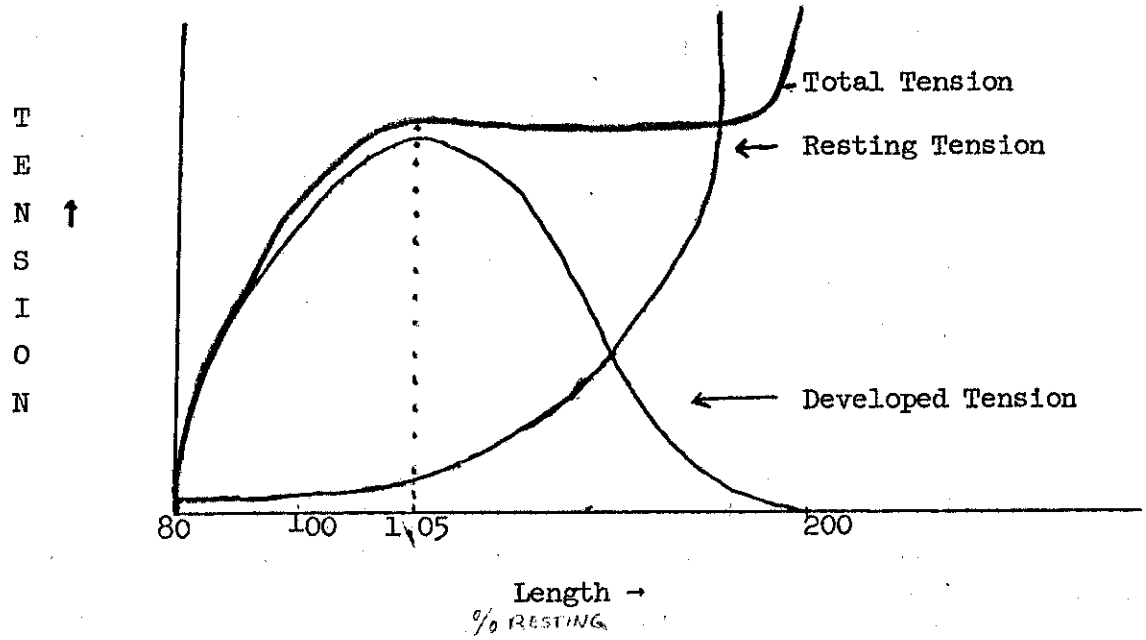


Figure 16.1 - Relation Between Length and Tension in Muscle

It can be seen that as the length of the muscle is increased, the resting tension increases approximately exponentially and the developed tension changes as perhaps a power function of the length. Certain important characteristics of these curves may be noticed. Say that the in sites resting length of muscle be designated at 100% length. Increasing or stretching the fiber or muscle to length 105% then is increasing the length 5% over the in sites resting length. It is noticed that at this length, the developed tension of the muscle reaches its highest value, and that on either side of this length the amount of tension which can be developed falls off. This means that the in sites resting length of muscle is near optimum for tension development or work performance. From the graph, it is also noticed that the resting tension increases at about the same length as the maximum tension, and increases then very gradually at the length at which the developed tension has declined to zero.

These curves may be explained in the following manner. In the first part of the curve, with the muscle shorter than resting length, the contraction of a single twitch is used to take up some of the slack in the series of the elastic components of the fiber - the actin slack. As the muscle is stretched, some of this slack is taken up mechanically, and the actual contraction of the components begin to cause tension development in the fiber. The tension development increases until at the length at which all the slack is mechanically taken up, at which length a contraction exerts a maximum tension effect. Further stretching results in an increase in the resting tension, so that with further increase in length, the total tension (resting and active) remains more or less constant, although the resting tension takes more and more a larger part of the total. Eventually, the resting tension alone equals the maximum developed tension, and at this length the developed tension falls to zero. Maximum tension is still present, but it is in the form of resting tension and cannot be added to by contraction. Further stretching results in further mechanical increases in tension, until the fiber breaks.

B. Summation of Contractile Response

Another type of phenomena which deals with an altered mechanical response is referred to as the summation of contractile response, or wave summation. Thus, if two impulses are delivered to a single muscle fiber or motor unit, in a period of time such that the second impulse falls during the contractile phase of the muscle, than a second response is induced which is greater than the first. The second impulse has caused a summated contractile response.

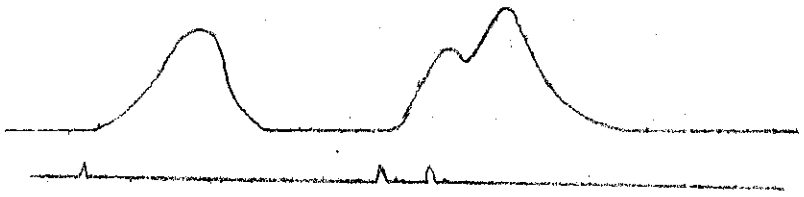


Figure 16.2 - A Summated Contractile Response

The explanation for this may be two fold. One, as a wave of contraction courses over a fiber, the contracting areas stretch somewhat the uncontracted portions, permitting only a certain amount of actual total shortening. A second wave, being present only partially during the same time as the first, will cause a further shortening, contracting a region of the fiber which would be normally stretched somewhat by the first wave. This would produce wave summation. Another factor may enter into the explanation. Apparently in a single twitch, the processes of recovery come into operation immediately after excitation of the actual contraction process, so that as contraction begins, relaxation processes are already damping the contraction response. A second stimulus, then, again activates the contractile response and delays the relaxation, so that contraction may occur to a greater degree, and result in what is termed wave summation.

Wave summation leads to tetanic contraction, in which relaxation does not occur at all, but the contractions are fused into a smooth continuous curve, the mechanical response being greater than during a single twitch for the reason indicated.

The character of muscle response may also be altered by the quantity of K^+ ions present in the fiber. An optimum range for this ion exists in the fiber (.05 -.12 M) and on each side of this optimum, the mechanical response of the fiber is depressed. The ion is concerned in some way with the association of actin and myosin.

As a muscle remains in an inactive state, it accumulates K^+ ions. Eventually the concentration is beyond the optimum range for contraction. A stimulus, therefore, produces a response which is below the maximum otherwise obtainable. During the twitch, K^+ flows out of the fiber and does not all reenter until some time has elapsed. If now, during this time, a second stimulus is given to the muscle, the response is greater, due to more optimum concentration of K^+ ions. This continues until the optimum contraction is reached. If activity is further sustained, too much K^+ is ~~the~~ lost and the response may decline. This phenomena of increasing response with increasing frequency of stimulus is referred to as the treppe effect, or staircase phenomena.

C. Fatigue and Rigor

At times, a persistent contracted state of the muscle may result from "fatigue", or may be induced by drugs such as veratrine, acetylcholine, etc. In this condition, nerve or electrode stimulation of the muscle does not play a part. The cause is in the failure of the muscle to relax, and results when the membrane is constantly depolarized by ACH or veratrine, the ionic balance not allowed to return to normal, or from an exhaustion of ATP and its energy reserve, CP. If the supply of these substances is depleted, then relaxation does not occur. Contraction persists and the state is called contracture. Contracture is reversible, providing the ATP or CP is restored or the membrane is allowed to repolarize.

One type of irreversible contraction is termed rigor. Rigor is the slow contraction and hardening of muscles which occurs after death. It is not attended by metabolic activity or electrical activity, and is precipitated by the breakdown of all the ATP and CP in muscle, followed by the permanent coagulation of the contractile units. Rigor may develop from ten minutes to seven hours after death. Heat, vigorous activity, fatigue, all accelerate the process by accelerating the speed of breakdown of ATP and CP. The condition disappears in one to six days, owing to the dissolution of the organic substances.

Muscle fatigue, a vague term, is defined as a diminished contractile response following a period of activity, completely reversible, following a period of rest. It is a transitory decrease in the working capacit y of muscle. The causes of fatigue are probably many, but are not known with any certainty. As has already been indicated, one prominent feature in fatigue may well be the loss of K^{+} ions from the muscle, as well as a loss of Ca^{++} and magnesium ions. Another cause which has been suggested is an interference with the metabolic reactions either yielding energy or utilizing the energy produced for contraction. pH changes are not thought to be of importance. In the intact muscle, much of the fatigue may occur not at the muscle ~~stuff~~, but rather at the myoneural junction, with the gradual depletion of acetylcholine at the end plate region. Thus, although with prolonged activity ~~of~~ both the junction and the muscle fatigue, the complete refractoriness is manifested by the myoneural junction first. In some instances, fatigue of muscle may lead to contracture.

CHAPTER 17

QUANTITATIVE DESCRIPTION OF A SINGLE MUSCLE TWITCH

The purpose of this chapter is to describe in a quantitative manner, mathematically, the time course changes of muscle length or tension development following the application of a single threshold excitatory stimulus to a muscle. A differential equation will be set up, based on a mechanical model for damped oscillatory motion, and using a chemical kinetic expression as the forcing function for the motion.

The contraction cycle of muscle can be considered as an oscillation of a damped system, the oscillation forced by chemical reactions. By way of introduction, consider first the manner in which equations of oscillation are derived.

A. Equations of Oscillation

Oscillations originate wherever there is an exterior force tending to bring a displaced system back to its equilibrium position. The most simple ("harmonic") form of oscillation occurs if the intensity of the restoring force is proportional to the distance from the equilibrium position.

Given a mass (Figure 7.1) which is able to move along the x-axis and which is being pulled back to its equilibrium position $x = 0$ by a weightless spring such that the restoring force is $P_x = -cx$. The motion is then characterized by the differential equation

$$m\, d^2x/dt^2 = -cx \qquad (7.1)$$

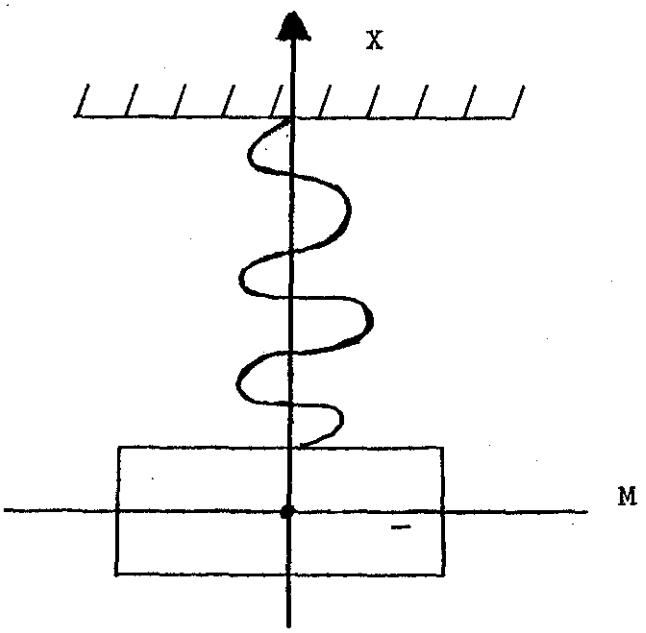


Figure 17.1 - Mass Attached to a Spring

For the exact determination of a single case, two given values of initial position and velocity, are required. If, for example, at the beginning the mass is displaced from the equilibrium position and then released without any initial velocity, we have for $t = 0$, $x = x_0$ and $dx/dt = 0$. If, on the other hand, the particle at its equilibrium position receives a blow at the time $t = 0$, we have at this instant: $x = 0$, $dx/dt = v_0$. In this example, it is possible to find the essential properties of the motion from the differential equation alone without the aid of the initial conditions.

The differential equation (17.1) is homogeneous and linear, that is, the unknown x or one of its derivatives is contained in the same power (the first) in every term. Differential equations of this type can be integrated directly (for any order and any number of unknowns) by using exponential functions. A solution of a differential equation of this

type is given by

$$x = Ae^{\alpha t}. \tag{7.2}$$

Here, A is an arbitrary constant of integration, whereas the constant α can be determined from the differential equation. Since the differential equation is homogeneous and linear, an arbitrary number of such solutions may be added and the sum is again a solution. The order of the equation determines the number of independent solutions, and the necessary number of constants of integration (in our case, two). We also can determine all the α's. For by introducing (7.2) in (7.1), we obtain

$$m\alpha^2 Ae^{\alpha t} = -cAe^{\alpha t},$$

and this is an algebraic equation for α since we can divide both sides by the exponential factor. The degree of the algebraic equation is determined by the order of the differential equation, and we thus obtain just the necessary number of solutions. In the above case

$$\alpha = \pm i\,(c/m)^{1/2}$$

and it follows that

$$x = Ae^{i(c/m)^{1/2}t} + Be^{-i(c/m)^{1/2}t}. \tag{7.3}$$

Using the well known formula

$$e^{\pm iy} = \cos y \pm i \sin y \tag{7.4}$$

We can write (7.3) in the form

$$\begin{aligned} x &= (A + B)\cos (c/m)^{1/2}t + i(A - B)\sin (c/m)^{1/2}t \\ &= C\cos (c/m)^{1/2}t + D\sin (c/m)^{1/2}t. \end{aligned} \tag{7.5}$$

Since the solution of the problem must be real, C and D are two real constants which can easily be determined from the initial conditions.

Assume that in addition to the restoring force which pulls the particle back to the equilibrium position, there is also a force acting due to friction. This resisting force may be proportional to the speed dx/dt (factor k). This, however, is not always the exact form of a resisting force, but in most cases can be used as an approximation. The differential equation is now the following:

$$m\, d^2x/dt^2 = -cx - k\, dx/dt \qquad (17.6)$$

This is again homogeneous and linear and integrable in the form $x = Ae^{\alpha t}$, and represents the equation for damped oscillatory motion (Figure 7.2 and 7.3).

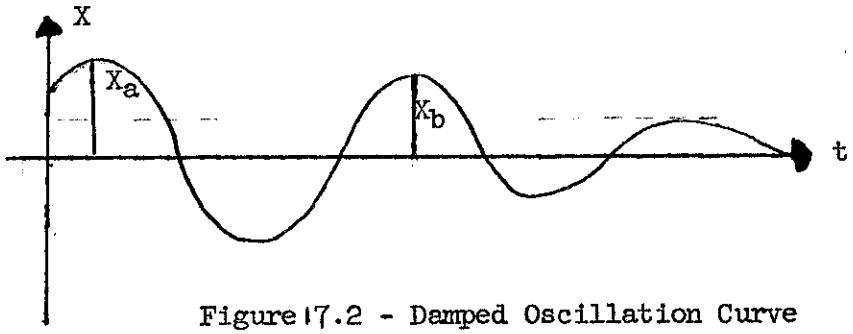


Figure 17.2 - Damped Oscillation Curve

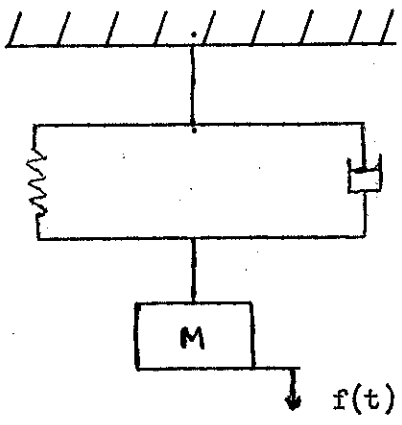


Figure 17.3 - Mechanical Model of Damped Oscillatory Motion

B. Forcing Function

Figure 7.3 also indicates the presence of a forcing function for the oscillation. In muscle, the tension development or shortening is determined by chemical reactions. For this analysis, the kinetic expression for two first order irreversible consecutive reactions will be used:

$$A \xrightarrow{\vec{k}_1} B \xrightarrow{\vec{k}_2} C$$

It is assumed that at time:0, a given amount of substance A is present in muscle, which, upon activation or stimulation, is transformed into substance B at rate k_1. It is further assumed that the amount of substance B present at any time is proportional to the shortening of the muscle, or to the tension developed. In order to include a forcing function in equation (7.6), it is necessary to find an expression for the amount of substance B present as a function of time. This is done as follows.

Set the concentration of A at any time = x, of B = y, and of C = z. By definition, and proved experimentally, a first order irreversible reaction is described by

$$-\frac{dx}{dt} = k_1 x, \tag{7.6}$$

or, the rate of disappearance of x, i.e., $-\frac{dx}{dt}$, is proportional at any time to the concentration of x.

Hence,

$$-\frac{dx}{x} = k_1(dt) \tag{7.7}$$

and,

$$-\int \frac{dx}{x} dt = \int k_1(dt)dt \tag{7.8}$$

$$-\ln x = k_1 t + C \tag{7.9}$$

To evaluate C, let $t = 0$, then $C = -\ell n\, x$. Also, at $t = 0$, $x = A_o$, the original amount of substance A present. Thus,

$$C = -\ell n\, A_o,$$

and,

$$-\ell n\, x = k_1 t + (-\ell n\, A_o),$$

or,

$$\ell n(x - A_o) = -k_1 t = \ell n\left(\frac{x}{A_o}\right),$$

and,

$$\frac{x}{A_o} = e^{-k_1 t}; \quad x = A_o e^{-k_1 t}. \tag{17.10}$$

This represents the concentration of x at any time.

The concentration of y at any time is determined as follows:

The rate of appearance of y, $\frac{dy}{dt}$, is dependent upon the concentration of x at any time, and upon the first velocity constant. Thus:

$$\frac{dy}{dt} = k_1 x.$$

The rate of disappearance of y, $-\frac{dy}{dt}$, is dependent upon the concentration of y at any time, and upon the second velocity constant. Thus:

$$-\frac{dy}{dt} = k_2 y.$$

But in two consecutive reactions, the actual rate of appearance of y is equal to $k_1 x$ minus its rate of disappearance, $k_2 y$.

Hence,

$$\frac{dy}{dt} = k_1 x - k_2 y. \tag{17.11}$$

Since,

$$x = A_o e^{-k_1 t},$$

Then,

$$\frac{dy}{dt} = A_o k_1 e^{-k_1 t} - k_2 y. \tag{17.12}$$

The solution of this equation is carried out as follows:

Let

$$y = UV.$$

Then,

$$\frac{d(UV)}{dt} = A_o k_1 e^{-k_1 t} - k_2 UV. \tag{17.13}$$

Recall that if $y = UV$, then $\frac{dy}{dt} = \frac{dUV}{dt} = U\frac{dV}{dt} + V\frac{dU}{dt}$.

Hence,

$$U\frac{dV}{dt} + V\frac{dU}{dt} + k_2 UV = A_o k_1 e^{-k_1 t},$$

$$U\left(\frac{dV}{dt} + k_2 V\right) + V\frac{dU}{dt} = A_o k_1 e^{-k_1 t} \tag{17.14}$$

Following standard procedure for solving first order linear differential equations, let $\frac{dV}{dt} + k_2 V = 0.$

Therefore, $\frac{dV}{V} = -k_2\, dt$

and,

$$\int \frac{dV}{V} = \ell n V = -k_2 t + C' \quad .$$

To evaluate C', let t = 0. Then, since at t = 0, V = V_o ,

$$C' = \ell n\, V_o$$

and,

$$\ell n\, V = -k_2 t + \ell n\, V_o ,$$

$$\ell n \left(\frac{V}{V_o}\right) = -k_2 t$$

$$\frac{V}{V_o} = e^{-k_2 t} , \quad V = V_o e^{-k_2 t} . \tag{17.15}$$

Returning to equation (17.14), and under the conditions where $\frac{dV}{dt} = -k_2 V$ or $\frac{dV}{dt} + k_2 V = 0$, then (17.14) becomes

$$V \frac{dU}{dt} = A_o k_1 e^{-k_1 t} . \tag{17.16}$$

Substituting the value of V from (7.15) into (7.16):

$$V_o e^{-k_2 t} \left(\frac{dU}{dt}\right) = A_o k_1 e^{-k_1 t} \tag{17.17}$$

and,

$$dU = \frac{A_o k_1 e^{-k_1 t}}{V_o e^{-k_2 t}} \, dt$$

$$= \frac{A_o k_1 e^{(k_2 - k_1) t}}{V_o} \, dt . \tag{17.18}$$

Integrating (7.18)

$$U = \frac{A_o k_1 e^{-(k_2 - k_1)t}}{V_o(k_2 - k_1)} + C'' \qquad (7.19)$$

Since $y = UV$, multiplying (7.19) by (7.15) gives:

$$UV = y = V_o e^{-k_2 t}\left[\frac{A_o k_1 e^{-(k_2 - k_1)t}}{V_o(k_2 - k_1)} + C''\right] \qquad (7.20)$$

To evaluate C", let $t = 0$, then $y = 0$, and

$$0 = V_o\left(\frac{A_o k_1}{V_o(k_2 - k_1)}\right) + C''V_o \qquad (7.21)$$

$$C'' = -\frac{A_o k_1}{U_o(k_2 - k_1)} \qquad (7.22)$$

Substituting back into (7.20),

$$y = V_o e^{-k_2 t}\left[\frac{A_o k_1 e^{t(k_2 - k_1)}}{V_o(k_2 - k_1)} + \frac{-A_o k_1}{V_o(k_2 - k_1)}\right] \qquad (7.23)$$

$$= e^{-k_2 t}\left(\frac{A_o k_1 e^{t(k_2 - k_1)} - A_o k_1}{k_2 - k_1}\right)$$

$$= \frac{A_o k_1 e^{-k_1 t} - A_o k_1 e^{-k_2 t}}{k_2 - k_1}$$

$$= \frac{A_o k_1}{k_2 - k_1}\left(e^{-k_1 t} - e^{-k_2 t}\right) \qquad (7.24)$$

Hence, the complete equation which describes a single muscle twitch is,

$$M\frac{d^2y}{dt^2} + R\frac{dy}{dt} + Ky = f(t) = \frac{pA_o k_1}{k_2 - k_1}\left(e^{-k_1 t} - e^{-k_2 t}\right). \qquad (7.25)$$

Where,

M = mass of muscle and recording system
y = shortening or tension development
t = time
R = damping coefficient of muscle and recording system
K = stiffness coefficient of muscle and recording system
p = proportionality constant
A_o = amount of A substance present at t = 0
k_1 = rate constant for conversion of A → Øβ
k_2 = rate constant for conversion of B → C.

The solution of (7.25), a second order linear differential equation, is presented in the next chapter.

CHAPTER 18

SOLUTION OF EQUATION DESCRIBING SINGLE MUSCLE TWITCH

The solution of (7.25), a second order linear differential equation with constant coefficients, is carried out as follows:

a. The equation is put into the general form

$$\frac{d^2y}{dt^2} + P\frac{dy}{dt} + Qy = f(t) \qquad (8.1)$$

Hench (7.25) becomes

$$\frac{d^2y}{dt^2} + \frac{R}{M}\frac{dy}{dt} + \frac{K}{M}y = \frac{1}{M}f(t) \qquad (8.2)$$

Let $\frac{R}{M} = 2a$, $\frac{K}{M} = Z$, and $\frac{1}{M} = C$, and thus

$$\frac{d^2y}{dt^2} + 2a\frac{dy}{dt} + Zy = Cf(t) \qquad (8.3)$$

b. Set

$$\frac{d^2y}{dt^2} + 2a\frac{dy}{dt} + Zy = 0 \qquad (8.4)$$

A general solution for this equation is

$$y = C_1e^{r_1t} + C_2e^{r_2t} \qquad (8.5)$$

c. The term r is evaluated by differentiating $y = e^{rt}$ twice, and substituting the results back into (8.4):

$$y = e^{rt}$$

$$\frac{dy}{dt} = re^{rt}$$

$$\frac{d^2y}{dt^2} = r^2e^{rt}$$

$$r^2e^{rt} + 2are^{rt} + Ze^{rt} = 0 \qquad (8.6)$$

Dividing (8.6) by e^{rt} gives

$$r^2 + 2ar + Z = 0 \qquad (8.7)$$

Equation (8.7) is called the auxiliary equation, and through the technique used to derive it, r can be found since (8.7) is a quadratic form.

d. Here

$$r = \frac{-2a \pm \sqrt{(2a)^2 - 4Z}}{2}$$

$$r = -a + \sqrt{a^2 - z} \quad \text{and} \quad -a - \sqrt{a^2 - z}$$

The complete solution of (8.4) is therefore:

$$y = C_1e^{\left(-a + \sqrt{a^2 - z}\right)t} + C_2e^{\left(-a - \sqrt{a^2 - z}\right)t} \qquad (8.8)$$

Equation (8.8) is the complementary solution of (8.3).

e. The complementary solution is further developed as follows: Consider the case where $\sqrt{a^2 - z}$ is imaginary. (If equation (8.3) represents oscillatory motion, where M = mass of system, R = damping coefficient, K = stiffness coefficient, and since $a = \frac{R}{2M}$, and $Z = \frac{K}{M}$, and since K is almost always much larger than R, the quantity $\sqrt{a^2 - z}$ will be imaginary.) Arrange (8.8) as

$$y = C_1 e^{-at + \sqrt{a^2 - z}\,t} + C_2 e^{-at - \sqrt{a^2 - z}\,t} \qquad (8.9)$$

and,

$$y = e^{-at}\left(C_1 e^{\sqrt{a^2 - z}\,t} + C_2 e^{-\sqrt{a^2 - z}\,t}\right) \qquad (8.10)$$

Recall that Euler's formula is

$$e^{ix} = \cos x + i \sin x$$

and,

$$e^{-ix} = \cos x - i \sin x$$

Let $i = \sqrt{a^2 - z}$, and $x = t$, so that (8.10) becomes:

$$y = e^{-at}\left[C_1(\cos t + \sqrt{a^2 - z}\,\sin t) + C_2(\cos t - \sqrt{a^2 - z}\,\sin t)\right] \qquad (8.11)$$

(8.11) is simplified as follows:

Let $$C_1 = \frac{1}{2}\left(A - B'\sqrt{a^2 - z}\right)$$

$$C_2 = \frac{1}{2}\left(A + B'\sqrt{a^2 - z}\right)$$

Thus, (8.11) becomes,

$$y = e^{-at}\left[\frac{1}{2}\left(A - B'\sqrt{a^2 - z}\right)\left(\cos t + \sqrt{a^2 - z}\sin t\right) + \right.$$

$$\left.\frac{1}{2}\left(A + B'\sqrt{a^2 - z}\right)\left(\cos t - \sqrt{a^2 - z}\sin t\right)\right]. \qquad (8.12)$$

Multiplying the quantities out, (8.12) reduces to:

$$y = e^{-at}\left(A\cos t - B'(a^2 - z)\sin t\right) \qquad (8.13)$$

Setting $B'(a^2 - z) = B$, (8.13) is

$$y = e^{-at}(A\cos t - B\sin t) \qquad (8.14)$$

This is the complete solution of (8.4) and the complementary solution of (8.3); the constants A and B are to be determined.

f. The complete solution of (8.3) is dependent upon the form of $f(t)$. Suppose that $f(t) = \frac{pA_o k_1}{k_2 - k_1}(e^{-k_1 t} - e^{-k_2 t})$, or the right hand of equation (8.3) can be written as: $C'e^{-k_1 t} - C'e^{-k_2 t}$. Successive integration of this expression will always lead to a form $\bar{W}\,e^{-k_1 t} - \bar{Z}\,e^{-k_2 t}$,

where $\bar{W}$ and $\bar{Z}$ are undetermined coefficients. A particular solution of (8.3) is therefore

$$y_p = \bar{W} e^{-k_1 t} - \bar{Z} e^{-k_2 t} . \qquad (8.15)$$

The general solution of the given equation, (8.3), is a combination of (8.15) and (8.14):

$$y = \bar{W} e^{-k_1 t} - \bar{Z} e^{-k_2 t} + e^{-at} (A \cos t - B \sin t). \qquad (8.16)$$

g. The undetermined coefficients of (8.16), $\bar{W}$, $\bar{Z}$, A, and B, are evaluated as follows:

Let $(A \cos t - B \sin t) = \bar{A}$. Then (8.16) is:

$$y = \bar{W} e^{-k_1 t} - \bar{Z} e^{-k_2 t} + \bar{A} e^{-at} . \qquad (8.17)$$

At $t = 0$, let $y = 0$, and (8.17) is $0 = \bar{W} - \bar{Z} + A$, $A = -(\bar{W} - \bar{Z})$. (8.17) is therefore:

$$y = \bar{W} e^{-k_1 t} - \bar{Z} e^{-k_2 t} - (\bar{W} - \bar{Z}) e^{-at} . \qquad (8.18)$$

Now differentiate (8.15) twice:

$$y = \bar{W} e^{-k_1 t} - \bar{Z} e^{-k_2 t} \qquad (8.15)$$

$$\frac{dy}{dt} = -k_1 \bar{W} e^{-k_1 t} + k_2 \bar{Z} e^{-k_2 t} \qquad (8.19)$$

$$\frac{d^2y}{dt^2} = k_1^2 \bar{W} e^{-k_1 t} - k_2^2 \bar{Z} e^{-k_2 t} \qquad (8.20)$$

Substitute these expressions into equation (8.3) giving:

$$k_1^2 \bar{W} e^{-k_1 t} - k_2^2 \bar{Z} e^{-k_2 t} + 2a\left[-k_1 \bar{W} e^{-k_1 t} + k_2 \bar{Z} e^{-k_2 t}\right] +$$

$$Z\left[\bar{W} e^{-k_1 t} - \bar{Z} e^{-k_2 t}\right] = C'(e^{-k_1 t} - e^{-k_2 t}) . \qquad (8.21)$$

Collecting the $\bar{W}$ and $\bar{Z}$ terms give:

$$\bar{W} e^{-k_1 t}\left[k_1^2 - 2ak_1 + Z\right] - \bar{Z} e^{-k_2 t} (k_2^2 + 2a k_2 + Z) =$$

$$C'e^{-k_1 t} - C'e^{-k_2 t} . \qquad (8.22)$$

It is apparent that C' must be:

$$C' = \bar{W} (k_1^2 - 2ak_1 + Z) = \bar{Z} (k_2^2 - 2ak_2 + Z) \qquad (8.23)$$

Hence,

$$\bar{W} = \frac{C'}{k_1^2 - 2ak_1 + Z} .$$

$$\bar{Z} = \frac{C'}{k_2^2 - 2ak_2 + Z} .$$

The solution of equation (7.25) can therefore be written as:

$$y = \bar{W} e^{-k_1 t} - \bar{Z} e^{-k_2 t} - (\bar{W} - \bar{Z}) e^{-\frac{Rt}{2M}} \qquad (8.24)$$

where

$$\bar{W} = \frac{C'}{k_1^2 - \frac{R}{M} k_1 + \frac{K}{M}} \quad \text{and} \quad \bar{Z} = \frac{C'}{k_2^2 - \frac{R}{M} k_2 + \frac{K}{M}}$$

and $C' = D = \frac{pA_o k_1}{M(k_2 - k_1)}$.

CHAPTER 19

ANALOG COMPUTER THEORY; SUMMING AMPLIFIERS

In actual practice, in order for a muscle twitch to be described quantitatively, as by equation (8.24), it is necessary to obtain an exact fit of a recorded twitch curve with the theoretical curve of equation (8.24). If this is done, then values for the rate constants, damping and stiffness coefficients of muscle are obtained. It is not an easy task, however, to match a twitch curve to equation (8.24) by hand, and therefore at this time, it is well to introduce the analog computer and its application to curve matching.

Computer summation of equation terms is discussed in this chapter, the integration of terms by the computer in Chapter 10 together with the procedure for generating exponential terms, and in Chapter 11, time and amplitude scaling for computers will be considered.

In solving a differential equation such as

$$\frac{d^2x}{dt^2} + 4\frac{dx}{dt} + 10x = 50 \sin x,$$

two fundamental operations are necessary; the summing of terms and integration. Hence, in an analog computer, there are two basic kinds of amplifiers: summing amplifiers for adding equation terms, and integrating amplifiers for integrating equation terms. Summing amplifiers will be discussed first.

In the following, a certain voltage is applied to the input grid of a summing amplifier, which is diagramed in Figure 9.1. The object of the discussion is to define the output voltage of the amplifier in terms of the input voltage and of the circuit elements of the figure.

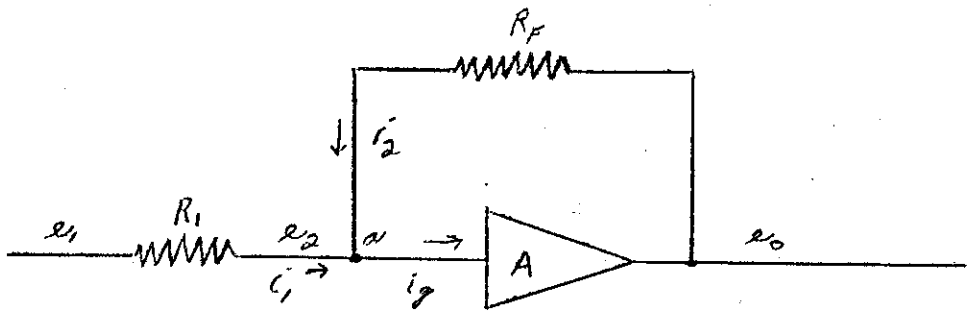


Figure 9.1 - Summing Amplifier

Consider the circuit diagram of Figure 9.1, where:

e_1 = "incoming" voltage to resistor R_1
R_1 = fixed resistance
e_2 = "outgoing" voltage from resistor R_1
A = high gain amplifier (50×10^6), with amplification = A
R_F = fixed feedback resistor across amplifier
e_o = output voltage of amplifier
i_1 = current from resistor R_1
i_2 = feedback current from amplifier
i_g = current drawn by grid of amplifier

Assume that the amplifier draws essentially no current from its input grid, so that

$$i_g = 0 .$$

From Kirchhoff's first law (the algebraic sum of the currents flowing toward any point in a network is zero), it is apparent that at

node point "a", $+ i_1 + (- i_2) = 0,$

or $$i_1 = i_2 . \tag{9.1}$$

(The sign of the input current is reversed by the amplifier.)

From Ohm's law,

$$i_1 = \frac{e_1 - e_2}{R_1} \tag{9.2}$$

and $$-i_2 = \frac{e_o - e_2}{R_F} , \tag{9.3}$$

or $$i_2 = \frac{e_2 - e_o}{R_F} . \tag{9.4}$$

Also, $$e_o = -Ae_2 . \tag{9.5}$$

From (9.1), (9.2), and (9.4),

$$\frac{e_1 - e_2}{R_1} = \frac{e_2 - e_o}{R_F} . \tag{9.6}$$

Substituting the value of e_2 from (9.5) into (9.6) gives:

$$\frac{e_1 + \frac{e_o}{A}}{R_1} = - \frac{\frac{e_o}{A} + e_o}{R_F} . \tag{9.7}$$

$$R_F e_1 + R_F \left(\frac{e_o}{A} \right) = -R_1 \left(\frac{e_o}{A} \right) - R_1 e_o$$

$$AR_F e_1 + R_F e_o = -R_1 e_o - AR_1 e_o$$

$$R_1 e_o + AR_1 e_o + R_F e_o = - AR_F e_1$$

$$e_o (R_1 + AR_1 + R_F) = - AR_F e_1$$

$$\frac{e_o}{e_1} = -\frac{AR_F}{(R_1 + AR_1 + R_F)}$$

$$= -\frac{\frac{AR_F}{R_1}}{\left(\frac{R_1}{R_1} + \frac{AR_1}{R_1} + \frac{R_F}{R_1}\right)}$$

$$= -\frac{\frac{R_F}{R_1} A}{\left(1 + A + \frac{R_F}{R_1}\right)}$$

$$= -\left(\frac{R_F}{R_1}\right) \frac{1}{\left(1 + \frac{1}{A} + \frac{R_F}{AR_1}\right)}$$

$$= -\frac{R_F}{R_1}\left[\frac{1}{1 + \frac{1}{A}\left(1 + \frac{R_F}{R_1}\right)}\right] \qquad (9.8)$$

Consider now equation (9.8) if R_F = 1 megohm, R_1 = 1 megohm, and $A = 50 \times 10^6$.

Then

$$\frac{e_o}{e_1} = -1\left[\frac{1}{1 + \frac{1}{50 \times 10^6} \times (2)}\right] \cong -1 .$$

Or, if R_F = 1 megohm, R_1 = 0.1 megohm, + $A = 50 \times 10^6$, then

$$\frac{e_o}{e_1} = -\frac{1}{0.1}\,(\,0.9999999\,)$$

$$\cong -10 .$$

It is apparent that in a summing amplifier, a very good approximation of the relation between input and output is as follows:

$$e_o = -\frac{R_F}{R_1} e_1 \qquad (9.9)$$

The value of an input voltage can thus be altered by changing the ratio of the feedback and input resistances.

It is also apparent that if the feedback resistance equals the input resistance, then $e_o = -e_1$; i.e., the sign of the voltage only is changed.

Consider now the situation where two or more inputs exist to the summing amplifier; as in Figure 9.2.

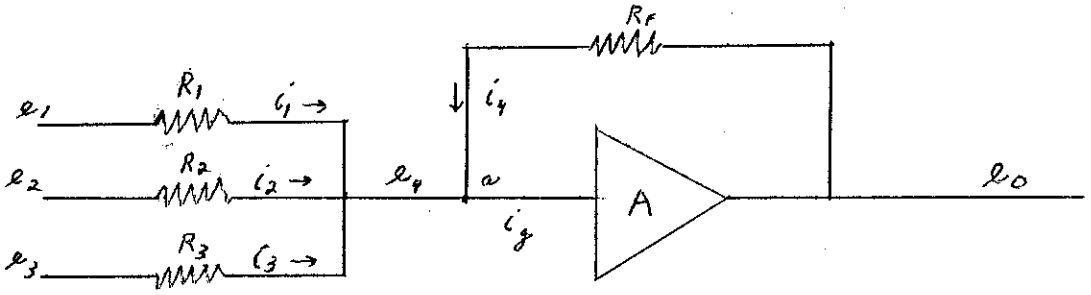


Figure 9.2 - Summing Amplifier With Three Inputs

As before, let $i_g = 0$, and

$$i_1 + i_2 + i_3 = i_4 \text{ at node a,}$$

or:

$$\frac{e_1 - e_4}{R_1} + \frac{e_2 - e_4}{R_2} + \frac{e_3 - e_4}{R_3} = \frac{e_4 - e_o}{R_F} \qquad (9.10)$$

Now, if $A = 50 \times 10^6$, and $e_o = 50 \times 10^6 e_4$, then

$$e_4 = \frac{e_o}{50 \times 10^6} .$$

If $e_o = 100$ volts, then $e_4 = \frac{100}{50 \times 10^6} = 0.000002$ volts.

In other words, consider that $e_4 = 0$. Hence, (9.8) becomes:

$$\frac{e_1}{R_1} + \frac{e_2}{R_2} + \frac{e_3}{R_3} = - \frac{e_o}{R_F}$$

$$e_o = - R_F \left(\frac{e_1}{R_1} + \frac{e_2}{R_2} + \frac{e_3}{R_3} \right) . \qquad (9.11)$$

Thus, the output voltage of a summing amplifier in the negative sum of the input voltages divided by each input resistance, and multiplied by the feedback resistance.

In Figure 9.2, if R_1, R_2, R_3, and R_F all equal 1 megohm, then

$$e_o = -(e_1 + e_2 + e_3).$$

Now suppose that three terms in an equation are to be summed, the three terms represented by voltage e_1, e_2, and e_3. Also suppose that e_1 is twice the value required by the equation, and that e_3 is only $\frac{1}{10}$ the value required. The value of e_2 is alright as stands. The three voltages can be summed in the required proportions by altering the values of each input resistor. Thus, let

e_1 = 20 volts (required = 10 volts)
e_2 = 10 volts
e_3 = 5 volts (required = 50 volts)

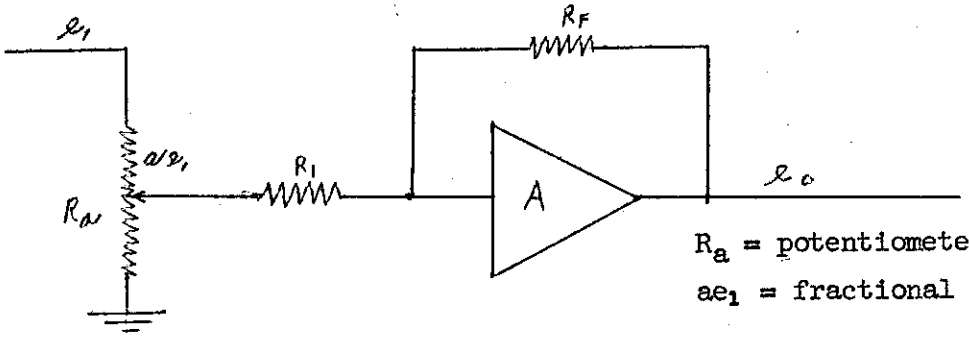
R_F = 1 megohm
R_1 = 2 megohms
R_2 = 1 megohm
R_3 = 0.1 megohm

Therefore,

$$e_o = -1\left(\frac{20}{2} + \frac{10}{1} + \frac{5}{0.1}\right)$$

$$= -70 \text{ volts, the correct and required sum.}$$

It will be noticed in this example that the input voltages are changed only by whole integers, not by fractions. This is because in the computer, the input and feedback resistors are fixed "whole numbers" in value. In practice, however, fractional voltage inputs are very commonly required, and these are achieved through the use of potentiometers which are placed in the circuit immediately before the input resistors. The potentiometers are variable resistors which fraction the incoming voltage between ground and the fixed input resistances. Thus fractional inputs can be obtained. The circuit connection is shown in Figure 9.3.



R_a = potentiometer resistance
ae_1 = fractional voltage of e_1

or, in schematic representation:

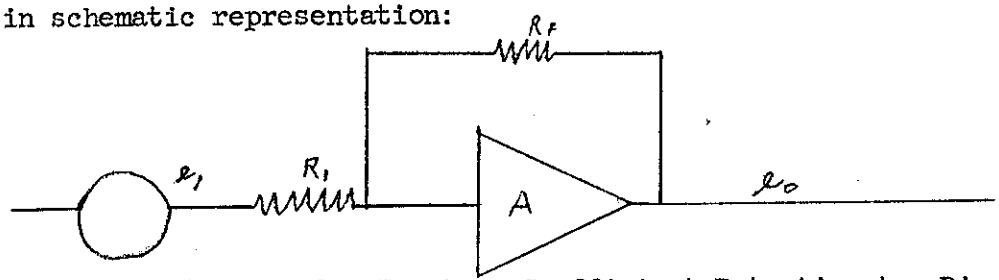


Figure 9.3 - Input or Coefficient Potentiometer Diagram

Adding a potentiometer to the circuit changes the relation between input and output voltages of equation (9.9) to

$$e_o = - \frac{aR_F}{R_1} e_1 , \tag{9.12}$$

and of equation (9.11) to

$$e_o = - R_F \left(\frac{a_1 e_1}{R_1} + \frac{a_2 e_2}{R_2} + \frac{a_3 e_3}{R_3} \right) . \tag{9.13}$$

In the above example of three input voltages to a summing amplifier, suppose that the actual input voltages required are $e_1 = 11.45$ volts, $e_2 = 7.63$ volts, $e_3 = 47.65$ volts. Since each voltage represents a term in an equation, the fractional component can be written as a coefficient of the variable of the term, as seen in the following table. (Assume that the values given each variable are values at a fixed instant of time.)

e Input Values	Required Values	Term	Variable Value	Coefficient Value	"a" Potentiometer Setting
$e_1 = 20$	11.45	$a_1 x$	10	1.145	0.1145
$e_2 = 10$	7.63	$a_2 y$	10	0.763	0.763
$e_3 = 5$	47.65	$a_3 z$	50	0.953	0.953

From equation (9.12), the values for the input and feedback resistors can be calculated.

$$e_o = - \frac{aR_F}{R_1} e_1$$

$$11.45 = - \frac{0.1145 \ (1)}{R_1} (20); \quad R_1 = 0.2 \text{ ohms.}$$

$$R_2 = - \frac{0.763 \ (1)}{7.63} \ (10) = 1$$

$$R_3 = - \frac{0.953 \ (1)}{47.65} \ (5) = 0.1 .$$

The output of the summing amplifier is therefore:

$$e_o = - R_F \left[\frac{a_1 e_1}{R_1} + \frac{a_2 e_2}{R_2} + \frac{a_3 e_3}{R_3} \right]$$

$$= - 1 \left[\frac{(0.1145)(20)}{.2} + \frac{(0.763)(10)}{1} + \frac{(0.953)(5)}{0.1} \right]$$

$$= - 66.73 \text{ volts, the required sum.}$$

It will be noticed that the actual potentiometer setting must always be less than 1. The negative sign of the above sum can be inverted by passing the output of the first amplifier through a second summing amplifier with a $\frac{R_F}{R_1}$ ratio of 1.

The above example constitutes a very indirect way of introducing the operation of a summing amplifier. A realistic example would be appropriate at this time.

Let it be desired to sum the following three terms:

1. $- 2 \times 10^3 a \frac{dy}{dt}$
2. $- 100 Zy$
3. $+ 100 Ce^{-.1K_1 t}$.

Let a, Z, and C be constants with the following values:

1. $a = 15.1$
2. $Z = 950$
3. $C = 9.6 \times 10^{-2}$.

The value of the coefficients of the terms therefore are:

1. $15.1 \times (-2 \times 10^3) = -30.2 \times 10^3$
2. $950 \times (-100) = -9.5 \times 10^4$
3. $9.6 \times 10^{-2} \times (100) = 9.6$.

Available as inputs to the summing amplifier are:

1. $-10^4 \frac{dy}{dt}$
2. $-10^4 y$
3. $+ e^{-.1K_1 t}$

The difference between the available input of a term and the actual desired term is remedied by means of a potentiometer and the input resistor.

Consider term 3.

The desired term is $9.6\ e^{-.1K_1 t}$. The available input is $e^{-.1K_1 t}$. If the potentiometer is set at 0.96, and a gain of 10 given to the input of this term, by making the $\frac{R_F}{R_1}$ ratio 10, then the required term is generated:

$$e_o = -\frac{(1)(0.96)}{0.1}\left(e^{-.1K_1 t}\right) = -9.6\ e^{-.1K_1 t} .$$

Note that the potentiometer setting is 10C.

In the second term, the ratio between the desired and available values is 9.5. Thus, a potentiometer setting of 0.95 and an amplifier gain of 10 will accomplish the desired end:

$$e_o = -\frac{(1)(0.950)}{0.1}\left(-10^4 y\right) = 9.5 \times 10^4 y .$$

Here, the potentiometer setting = 0.001Z.

In the third term, the ratio between desired and available values is $\frac{3.02 \times 10^4}{10^4} = 3.02$. If the potentiometer is set at 0.302, and an amplifier gain of 10 is made, then

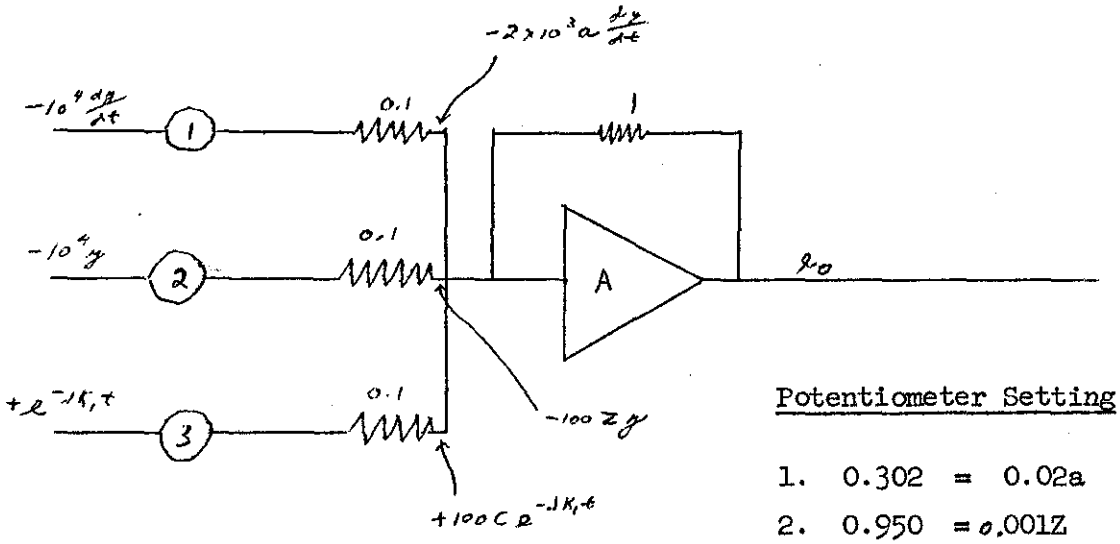
$$e_o = -\frac{(1)(0.302)}{0.1}(10^4) = 3.02 \times 10^4 = 30.2 \times 10^3.$$

Here, the potentiometer setting is 0.02a.

The problem is set up in tabular form as follows:

Desired Term	Value of Constant	Value of Coefficient	Available Input	Coefficient Ratio Desired/Available	Potentiometer Setting	Gain Required	$\frac{R_F}{R_1}$	Equivalent Potentiometer Setting
$-2 \times 10^3 a \frac{dy}{dt}$	15.1	-3.02×10^4	$-10^4 \frac{dy}{dt}$	$\frac{3.02 \times 10^4}{10^4} = 3.02$	0.302	10	$\frac{1}{0.1}$	0.02a
$-100Zy$	950	-9.5×10^4	$-10^4 y$	$\frac{9.5 \times 10^4}{10^4} = 9.5$	0.950	10	$\frac{1}{0.1}$	0.001Z
$100Ce^{-.1K_1 t}$	9.6×10^{-2}	9.6	$e^{-.1K_1 t}$	$\frac{9.6}{1} = 9.6$	0.960	10	$\frac{1}{0.1}$	10C

It is diagramed as follows:



Potentiometer Setting

1. 0.302 = 0.02a
2. 0.950 = 0.001Z
3. 0.960 = 10C

$$e_o = -1\left[\frac{(0.302)(-10^4\frac{dy}{dt})}{0.1} + \frac{(0.950)(-10^4y)}{0.1} + \frac{(0.960)(e^{-.1K_1t})}{0.1}\right]$$

$$= 2\times10^3 a\frac{dy}{dt} + 100Zy - 100Ce^{-.1K_1t}.$$

CHAPTER 10

ANALOG COMPUTER THEORY, CONTINUED

A. Integrating Amplifiers

An integrating amplifier of an analog computer is an amplifier which will integrate input voltages as a function of time. Its operation is as follows:

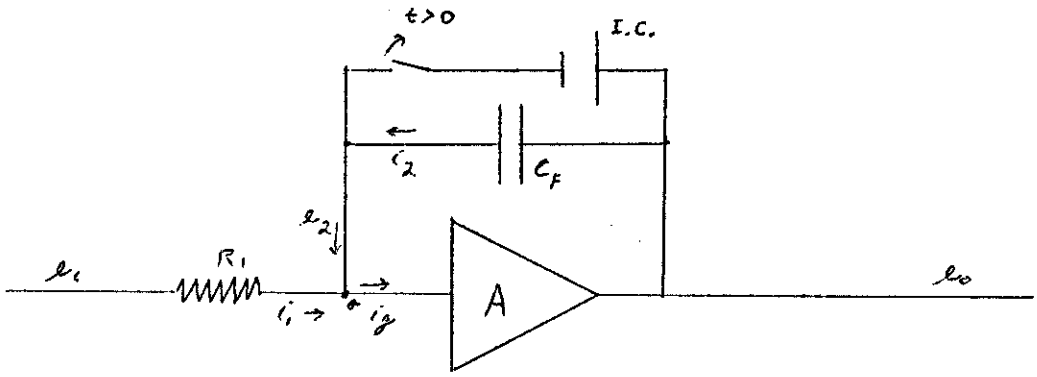


Figure 10.1 - Integrating Amplifier

It will be noticed in Figure 10.1 that the feedback resistance of the summing amplifier has been replaced by a feedback capacitor. In addition, a variable EMF across the amplifier is added, so that at time equal or less than zero, a certain initial charge can be put on C_F. This circuit is broken at t = 0, and thus initial condition voltages are introduced into the circuit. For time > 0, at node point "a", $i_1 + (-i_2) = i_g$,

$$\text{and } \frac{e_1 - e_2}{R_1} + C_F \frac{d(e_o - e_2)}{dt} = i_g . \qquad (10.1)$$

(Recall that the current flow from a capacitor equals the capacitance times the change of plate voltage per unit time, $I_c = C \frac{dv}{dt}$.)

As before, assume $i_g \cong 0$. Then equation (10.1) becomes:

$$\frac{e_1}{R_1} + C_F \frac{de_o}{dt} = 0 . \qquad (10.2)$$

Solving (10.2) for e_o,

$$C_F \int \frac{de_o}{dt}\, dt = -\int \frac{e_1}{R_1}\, dt$$

$$e_o = -\frac{1}{R_1 C_F} \int e_1 dt + C . \qquad (10.3)$$

From (10.3), it is apparent that the output voltage is the integral of the input voltage, times a gain factor, $-\frac{1}{RC_F}$, and plus a constant C. At time = 0, the input voltage e_1 is 0, so that $C = e_o$ at t = 0. The value of e_o at t = 0 is the voltage applied to C_F by the initial conditions circuit. Hence, C represents the initial conditions voltage, and is zero only if I. C. = 0. Figure 10.2 shows the situation for more than one input to an integrator.

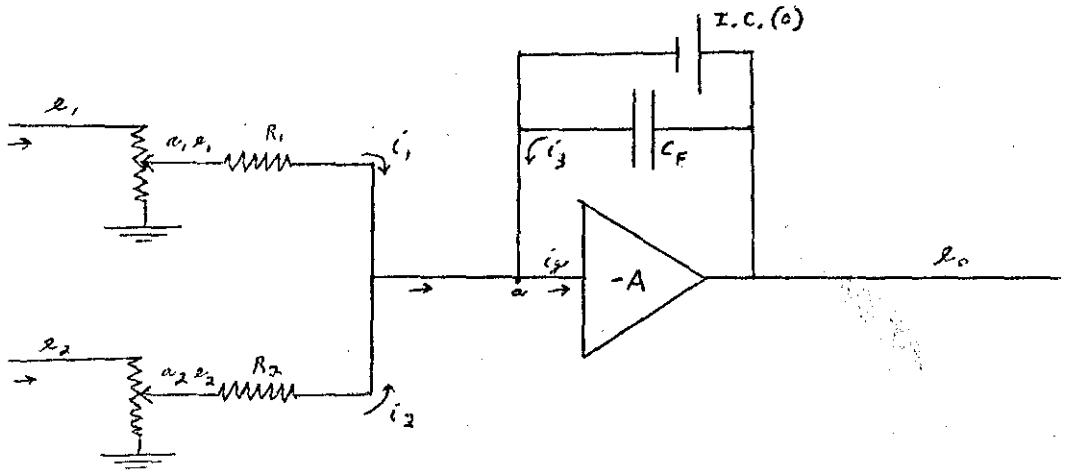


Figure 10.2 - Integrating Amplifier; Two Inputs Through Potentiometers

In Figure 10.2,

$$i_1 + i_2 + (-i_3) = i_g$$

and, $$\frac{a_1 e_1}{R_1} + \frac{a_2 e_2}{R_2} + C_F \frac{de_o}{dt} = 0 .$$

Hence, $$C_F \int \frac{de_o}{dt}\, dt = -\frac{a_1}{R_1} \int e_1\, dt - \frac{a_2}{R_2} \int e_2 dt + C$$

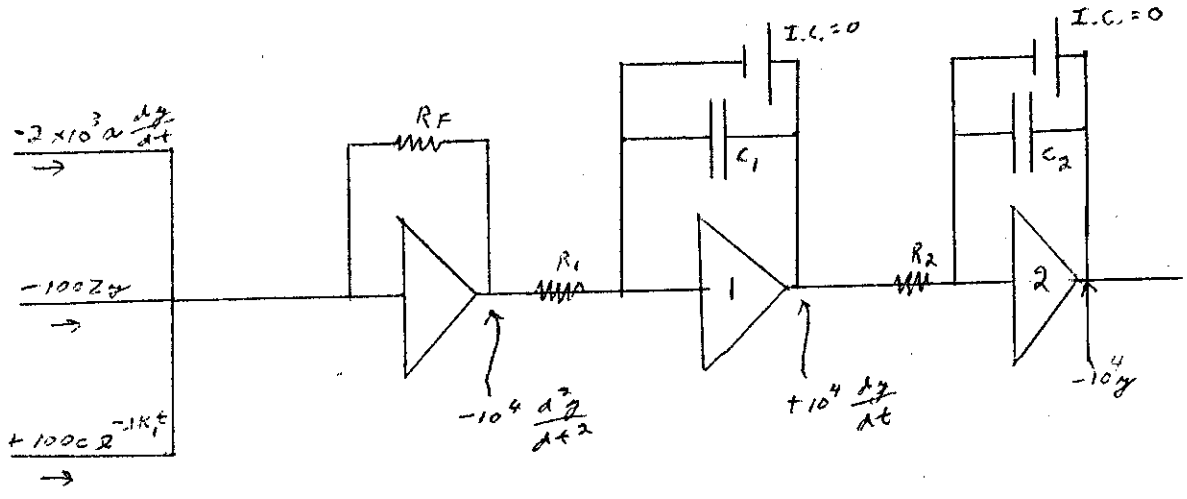
and, $$e_o = -\left[\frac{a_1}{R_1 C_F} \int e_1\, dt + \frac{a_2}{R_2 C_F} \int e_2 dt\right] + C . \qquad (10.4)$$

The following example will illustrate the use of integrating amplifiers. Given:

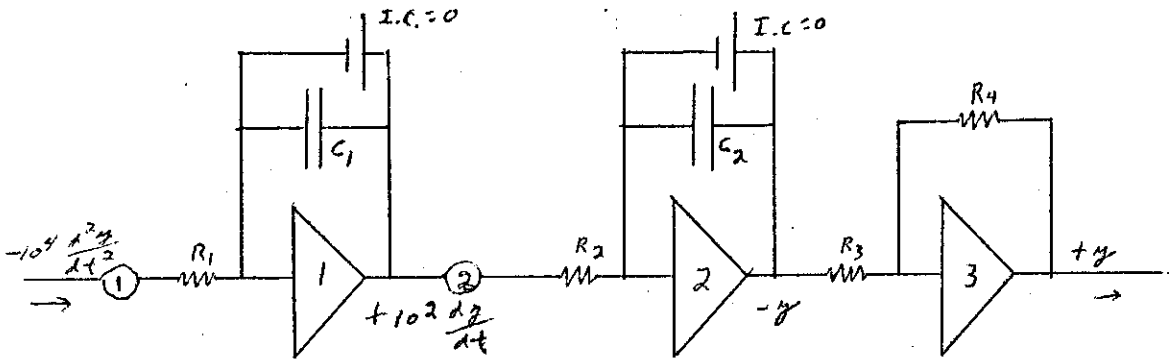
$$10^4 \frac{d^2y}{dt^2} + 2 \times 10^3 a \frac{dy}{dt} + 100Zy = 100\, ce^{-.1K_1 t} ,$$

or, $$10^4 \frac{d^2y}{dt^2} = -2 \times 10^3 a \frac{dy}{dt} - 100Zy + 100\, ce^{-.1K_1 t} . \qquad (10.5)$$

Let the problem be to find y in (10.5). In the example given in the section on summing amplifiers, the three right-hand terms of equation (10.5) were summed. Their sum is equal to the second derivative of y, so that the output of the summing amplifier can be used as the input to an integrator, and the output of the integrator can be used as the input to a second integrator, giving y, as follows:



where R_1, R_2, C_1, and C_2 all equal 1 megohm or 1 microfarad, and y = 0 at t = 0. Here, straight integrations were performed, with no change in gain and no potentiometers necessary. If it is desired to let e_o equal y exactly (no coefficient; positive sign), then the output of the summing amplifier can be handled as follows:



where	Pot ①	=	0.1	Pot ②	=	0.1
	R_1	=	10	R_2	=	10
	C_1	=	1	C_2	=	1
	R_3	=	1	R_4	=	1

The output of amplifier 1 is:

$$e_o = -\frac{a_1}{R_1 C_1} \int e_1 \, dt$$

$$= -\frac{0.1}{10} \left(-10^4 \frac{dy}{dt}\right)$$

$$= +10^3 \frac{dy}{dt} .$$

The output of amplifier 2 is:

$$e_o = -\frac{0.1}{10}\left(+10^2 y\right)$$

$$= -y \ .$$

B. Generating Exponential Functions

The forcing function of a muscle contraction very likely is the result of chemical kinetics, and exponential in nature. Exponential functions are generated by the computer in the following way:

Recall that if $y = e^{-K_1 t}$

then, $$\frac{dy}{dt} = -K_1 e^{-K_1 t}$$

and, $$\int \frac{dy}{dt}\,dt = \int -K_1 e^{-K_1 t}\,dt = e^{-K_1 t} \ .$$

Thus, if the input to an integrator is:

$$-K_1 e^{-K_1 t} \ ,$$

the output of the amplifier, with the amplifier sign change, would be:

$$-e^{-K_1 t} \ .$$

It is readily apparent that this output, multiplied by K_1, can be used as the amplifier input. Therefore, conditions are set so that

$$\frac{a}{RC_F} = K_1 \ .$$

Figure 10.3 shows the general diagram for generating $-e^{-K_1 t}$.

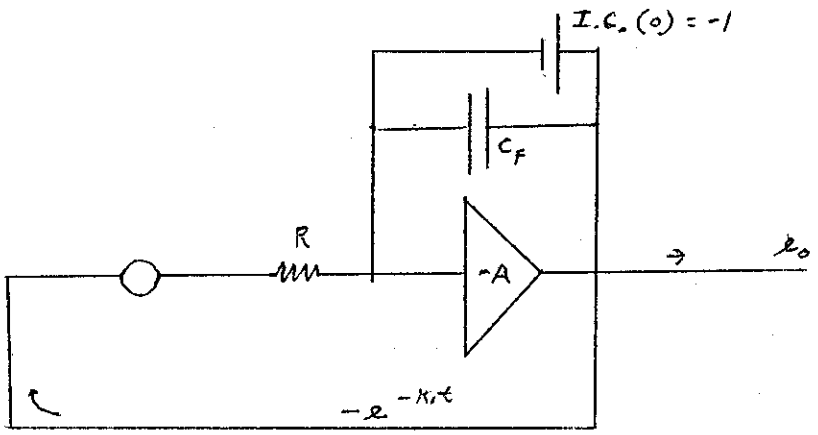


Figure 10.3 - Generation of $-e^{-K_1 t}$, Where $K_1 = \frac{a}{RC_F}$.

In Figure 10.3, if $K_1 = 0.5$, then $\frac{a}{RC_F} = 0.5$; a could equal 0.5, $R = 1.0$, and $C_F = 1.0$.

The output voltage of the set up in Figure 10.3 is:

$$e_o = -\frac{a}{RC_F}\int_o^t e_1 {}^{-K_1 t} dt + c \qquad (10.6)$$

$$= -0.5\int_o^t -e^{-0.5t} dt + c$$

$$= \left[-0.5\,\frac{-e^{-0.5t}}{-0.5}\right] - \left[-0.5\,\frac{-1}{-0.5}\right] + c$$

$$= -e^{-0.5t} + 1 + c. \qquad (10.7)$$

In the above equations, c is an arbitrary constant of integration equal to the value of e_o at $t = 0$. It is apparent that at $t = 0$, $e_o = -1$, and thus, I. C. (0) = -1.

Equation (10.6) therefore becomes:

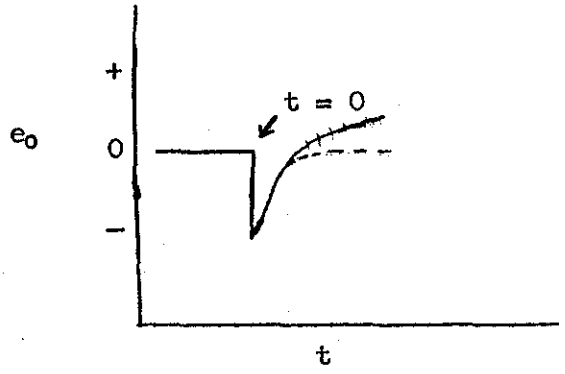
$$e_o = -K_1 \int_o^t dt + c = -e^{-K_1 t} \quad . \qquad (10.8)$$

$-e^{-K_1 t}$

It is of interest to note the range through which e_o of Figure 10.3 varies from $t = 0$ to $t = \infty$.

At $t = 0$, $e_o = -1$
$t = 1$, $e_o = -0.606$
$t = 2$, $e_o = -0.368$
$t = \infty$, $e_o = 0$

Thus, e_o varies from -1 volt to zero.



If it desired to generate $+e^{-K_1 t}$ then

$$e_o = -\frac{a}{RC_F} \int_o^t e^{-K_1 t} dt + c,$$

and if $K_1 = 0.5$, then

$$e_o = -0.5 \int_o^t e^{-0.5t} dt + c$$

$$= \left[-0.5 \frac{e^{-0.5t}}{-0.5}\right] - \left[-0.5 \frac{1}{-0.5}\right] + C$$

$$= e^{-0.5t} - 1 + C.$$

At $t = 0$, $e_o = 1$, thus $C = 1$, I.C.(0) = +1. In this instance, e_o varies from +1 at $t = 0$ to 0 at $t = \infty$.

The influence of changing the initial condition voltage on the output of the integrator is as follows:

If I.C.(0) = -100 volts, then $e_o = -100$ at $t = 0$. Yet, according to (10.8),

$$e_o = -e^{-K_1 t},$$

and here at $t = 0$, $e_o = -1$. Therefore, for $e_o = -100$ at $t = 0$, equation (10.8) must be altered to read:

$$e_o = -Ae^{-K_1 t}$$

where A = 100; i.e, the magnitude of the voltage change has been increased by a factor of 100. Thus, (10.7) becomes:

$$e_o = -0.5 \int_o^t - 100e^{-0.5t} dt + c$$

$$= \left[-0.5\ (100)\ \frac{-e^{-0.5t}}{-0.5}\right] - \left[-0.5\ (100)\ \frac{-1}{-0.5}\right] + c$$

$$= -100\ e^{-0.5t} + 100 + c$$

$$= -100e^{-0.5t} \qquad \text{where } C = -100$$

e_o varies in this instance from -100 volts at $t = 0$ to 0 at $t = \infty$.

Likewise, with I.C.(0) = +100 volts,

$$e_o = +100e^{-0.5t}.$$

Now, consider the case where it is desired to generate the function:

$$(e^{-K_1 t} - e^{-K_2 t}).$$

This can be done simply by generating $-e^{-K_1 t}$ and $+e^{-K_2 t}$, and then summing the two terms. The summing amplifier will change the signs to:

$$+e^{-K_1 t} \text{ and } -e^{-K_2 t}, \qquad \text{giving } e^{-K_1 t} - e^{-K_2 t}.$$

Figure 10.4 shows the diagram generating this function.

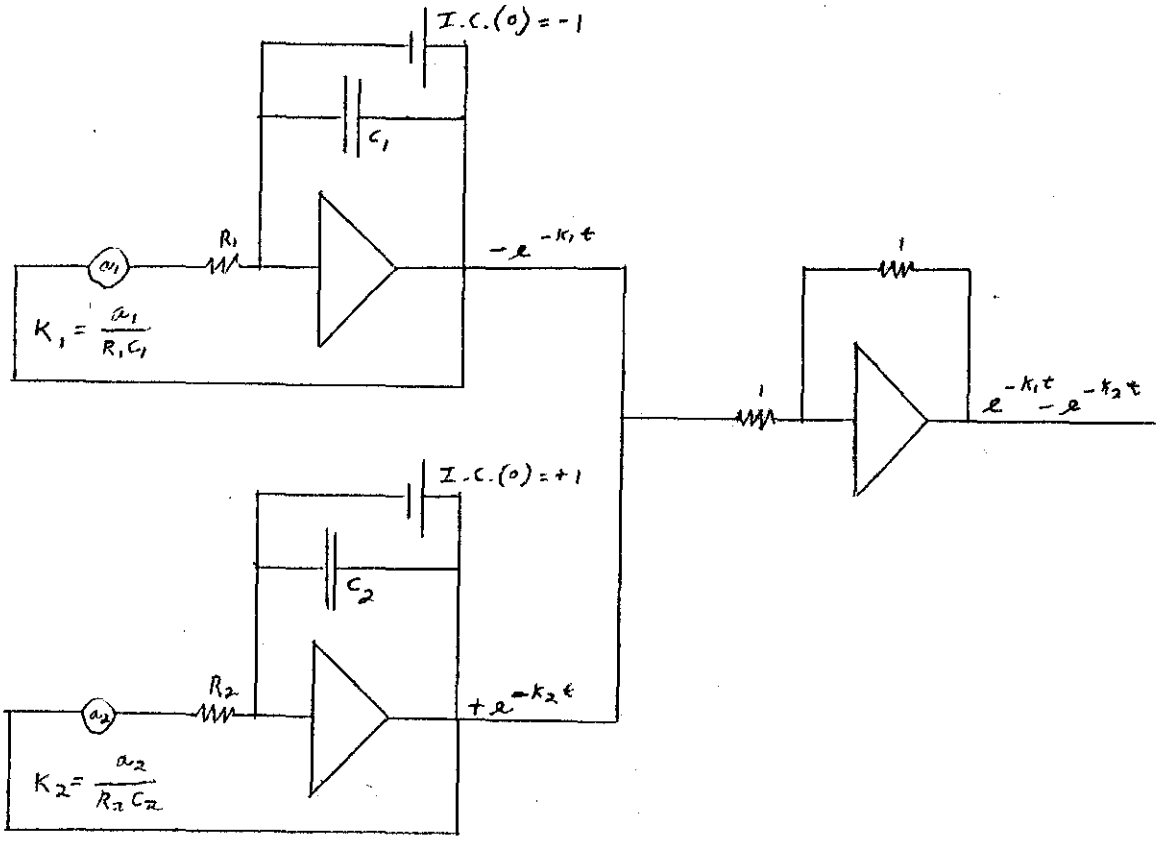


Figure 10.4 - Generation Of ($e^{-K_1 t} - e^{-K_2 t}$)

If in Figure 10.4, the initial conditions are + and − 100 volts, then the function generated is:

$$100 \left(e^{-K_1 t} - e^{-K_2 t} \right).$$

CHAPTER 11

ANALOG COMPUTER THEORY, CONCLUDED

A. Time Scale Changes of Basic Equations for Computer Solution

The frequency of a system under study may be too high or too low for computer operation or for recording. If so, it is necessary to adjust the time scale of the system equations. Errors in integrations are accentuated by low frequency systems, whereas high frequencies result in a phase shift in the operational amplifiers, or may be too fast for the dynamics of recording devices.

A heart muscle twitch is a system of relatively low frequency: 4 to 10 cycles per second. If a galvanometer-driven recorder or an oscilloscope is used as a computer readout device, these frequencies are not limiting. If a servo-driven recorder is used, the problem frequency must be cut down to 0.1 - 0.5 cps.

Many computer amplifiers will show a phase shift at about 20 radians/sec. $\tilde{=}$ 3 cps. The Donner amplifier, however, shows less than 0.2 degrees shift at 1000 cps. Also, this amplifier shows no distortion of 100 volts up to 700 cps. Therefore, the natural damped frequency of a heart muscle twitch should provide no distortion when directly handled by a Donner Computer, and the system equations should not require time scaling. It may be desirable at times, however, to slow the computer solution so that accurate readings of the value of various equation terms may be made during a twitch cycle. The manner of performing time scale changes is as follows:

An ordinary second order differential equation of the type

$$M \frac{d^2y}{dt^2} + C \frac{dy}{dt} + Ky = f(t) \qquad (11.1)$$

can be written as:

$$\frac{d^2y}{dt^2} + 2\zeta\omega_n \frac{dy}{dt} + \omega_n^2 y = f(t) \qquad (11.2)$$

where,

ω_n = undamped natural frequency in radians/sec.

ζ = damping ratio, of actual damping to the critically damped situation.

It is apparent from (11.1) and(11.2) that

$$\omega_n = \sqrt{\frac{K}{M}} \quad .$$

(The relation between linear frequency and angular frequency of a system with zero damping is:

$$f = \frac{\omega}{2\pi} = \frac{1}{2}\pi\sqrt{\frac{K}{M}}$$

where f = linear frequency in cps. A single muscle twitchis considered as one complete oscillation, one cycle.)

In performing a time scale change in an equation, each time containing term is multiplied by a factor "a". The new "time" is designated by τ, so that

$$\tau = at.$$

Note that

$$\frac{dy}{dt} = \frac{dy}{d(\frac{\tau}{a})} = a\frac{dy}{d\tau}$$

and $$\frac{d^2y}{dt^2} = \left(\frac{dy}{dt}\right)\left(\frac{dy}{dt}\right) = a^2 \frac{d^2y}{d\tau^2}$$

and $$\frac{d^ny}{dt^n} = a^n \frac{d^ny}{d\tau^n} .$$

A numerical example of a time scale change is as follows:

If $$\frac{d^2y}{dt^2} + 2a\frac{dy}{dt} + Zy = C(e^{-K_2t} - e^{-K_1t}) \qquad (11.3)$$

where $Z = 939.83$

then $\omega_n = \sqrt{939.83} = 30.6$ radian/sec.

If this is too fast for the desired computer solution, it may be slowed down by a factor of 10; then

$$t = \frac{\tau}{10}$$

and $$\frac{dy}{dt} = 10\frac{dy}{d\tau}, \quad \frac{d^2y}{dt^2} = 100\frac{d^2y}{d\tau^2} .$$

Equation (11.3) now becomes:

$$100\frac{d^2y}{d\tau^2} + 20a\frac{dy}{d\tau} + Zy = C(e^{-.1K_2\tau} - e^{-.1K_1\tau}) \qquad (11.4)$$

The undamped natural frequency of the new equation is:

$$\omega_n = \sqrt{\frac{939.83}{100}} = 3.06 \text{ radians/sec. machine time.}$$

If the initial conditions of equation (11.3) are:

$$y = 0, \quad \frac{dy}{dt} = 0 \text{ at } t = 0,$$

then the new initial conditions of equation (11.4) are unchanged:

$$y = 0, \quad \frac{dy}{d\tau} = 0 \text{ at } \tau = 0.$$

But if $y = 0, \quad \frac{dy}{dt} = 10$ at $t = 0$, then

$$y = 0, \quad \frac{dy}{d\tau} = 1 \text{ at } \tau = 0 \text{ since } \frac{dy}{dt} = 10\,\frac{dy}{d\tau}.$$

With this time scale change, a muscle twitch which is completed in 250 msec. of real time will now be completed in 2.5 sec. of computer time. Real and computer time recordings can be made to coincide if the muscle twitch records are made with a paper speed ten times that for recording the computer solution. Thus, the same records will be recorded during the same paper distance.

Note that the frequency with zero damping of a muscle twitch, according to equation (11.3), is:

$$f = \frac{\omega}{2\pi} = \frac{30.6}{6.28} = 4.8 \text{ cycles/sec.},$$

or each twitch would last approximately 200 msec. When stimulated at a rate of 1/sec., each twitch lasts for a little longer than 200 msec., the difference due to damping.

B. Amplitude Scale Changes of Basic Equations

The physical units of system are expressed in terms of voltage outputs of the computer amplifiers. If a muscle shortens 200 mm, and each computer volt is set equal to 1 mm, then the amplifiers will be overloaded, since the output voltage of each amplifier should be kept within ± 100 volts and away from zero. It is good practice to keep all

peak voltages near ± 50 volts. In the above example of muscle shortening, amplitude scaling would have to be performed on the descriptive equation, such that, perhaps, each mm shortening = 0.25 volts, or 1 volt = 4 mm shortening. Thus, 200 mm of shortening would be represented by 50 volts.

The voltage present in a computer circuit is determined basically by the initial conditions of the problem, and by the magnitude of the driving or forcing functions. Before amplitude scaling can be done, it is necessary to know or approximate the magnitude of the variables in the equations. This is done as follows:

Consider the following equation:

$$\frac{d^2y}{dt^2} + 2a\frac{dy}{dt} + Zy = C(e^{-K_2t} - e^{-K_1t}), \tag{11.5}$$

where y = the amount of shortening of the muscle. Experimentally, let it be known that the maximum value of y, y (max), equals 0.001 cm.

The natural undamped frequency of (11.5) is:

$$\omega_n = \sqrt{Z} \quad .$$

If $Z = 940$, then $\omega_n = 30.6$ radians/sec.

As a general principle, if ω_n is greater than unity, then $\frac{dy}{dt}_{(max)}$ is proportionally greater than y (max). If ω_n is less than unity, then $\frac{dy}{dt(max)}$ is proportionally less than y.

In the above example, if $\omega_n = 30$, then $\frac{dy}{dt(max)} = 30 \times y(max)$

$$= 30 \times 0.001 = .030.$$

Likewise, $\frac{d^2y}{dt^2}_{(max)} = \omega_n^2 \times y(max)$, if $\omega_n > 1$.

Thus: $\frac{d^2y}{dt^2(max)} = 900 \times 0.001 = 0.90$

and, $y\ (max) = 0.001$

$\frac{dy}{dt(max)} = 0.030$

$\frac{d^2y}{dt^2(max)} = 0.90$

NOTE: The validity of the above method for establishing maximum values of variables is seen in the following:

If $y = \sin \omega t$

then $\frac{dy}{dt} = \omega \cos \omega t$

and $\frac{d^2y}{dt^2} = -\omega^2 \sin \omega t.$

Since the maximum value of sin and cos = 1, it is apparent that

$$\frac{dy}{dt(max)} = \omega\ y\ (max)$$

and $$\frac{d^2y}{dt^2(max)} = \omega^2\ y\ (max)\ .$$

Therefore, if the physical problem is oscillatory in nature, then the maximum values of the variables and their derivatives may be determined from the undamped natural frequency of the system.

If damping is present in the system, then the maximum values of the derivatives found by this method are too large, since damping decreases the frequency.

In equation (11.5), the forcing function for muscle shortening is:

$$C(e^{-K_2 t} - e^{-K_1 t})\ .$$

The magnitude of the forcing function determines, of course, the magnitude of the contraction. Since the above expression contains a proportionality factor which renders the expression equivalent to the muscle shortening, its maximum value therefore equals the maximum value of y, which is 0.001 unit.

In equation (11.5) therefore, the maximum values of the terms are:

$$y = 0.001$$

$$\frac{dy}{dt} = 0.03$$

$$\frac{d^2y}{dt^2} = 0.90$$

$$C(e^{-K_2 t} - e^{-K_1 t}) = 0.001$$

$$e^{-K_2 t} = 1$$

$$-e^{-K_1 t} = -1 .$$

The e terms of the equation are generated by separate amplifiers so that their maximum values should be known. As is obvious, they vary from ±1 to 0.

CHAPTER 12

QUANTITATIVE ANALYSIS OF A MUSCLE TWITCH; DETERMINATION OF THE EFFECTIVE MASS, DAMPING AND STIFFNESS COEFFICIENTS

A. Theory

Assume that the muscle twitch is being recorded by means of a strain gage. The gage arm, with or without the connecting lever, will probably have a motion of oscillation which can be described by the equation:

$$m\ddot{y} + \beta\dot{y} + ky = 0 .$$

For damping below critical, $\beta < 2\sqrt{km}$, the frequency of oscillation is given by:

$$\omega = \sqrt{\frac{k}{m} - \frac{\beta^2}{4m^2}} .$$

The successive maximum distances, in absolute values, from the equilibrium position, are given by:

$$y_n = C\, e^{-\frac{\beta t_n}{2m}} \sqrt{1 - \frac{\beta^2}{4mk}} .$$

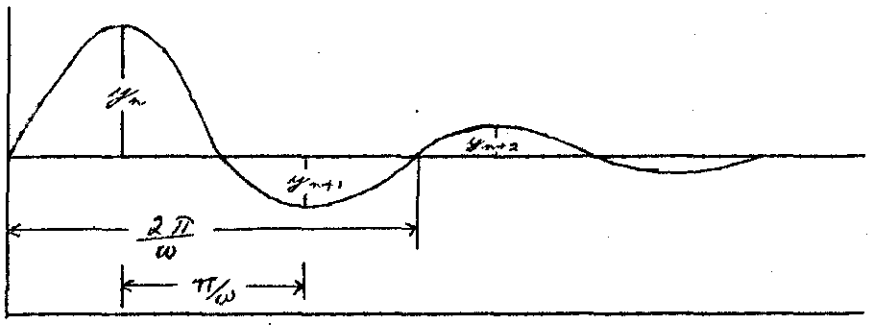
The ratio of two successive maximum values of y is given by:

$$\frac{y_n + 1}{y_n} = e^{-\frac{\beta \pi}{2m\omega}} .$$

The logarithmic decrement of the oscillation is therefore given by:

$$\xi = \ln\left(\frac{y_n + 1}{y_n}\right) = \ln y_n + 1 - \ln y_n = \frac{\beta \pi}{2m\omega} .$$

For clarification, the displacements y_n and $y_n + 1$ are indicated on the following curve:



If the ratio between y_n and $y_n + 2$ is to be determined, then the logarithmic decrement is given as:

$$\xi = \ln\left(\frac{y_n + 2}{y_n}\right) = -\frac{\beta \pi}{m \omega} .$$

In general, the logarithmic decrement term per se is the quantity $\frac{\beta}{2 m}$. When it is used in an equation with the ratios of maximum displacements, it is multiplied by the period covered by the displacements, as $\frac{\pi}{\omega}$ for successive + and − displacements giving $\frac{\pi \beta}{2 m \omega}$, or $\frac{2 \pi}{\omega}$ for successive + + displacements giving $\frac{\beta}{2m} \times \frac{2 \pi}{\omega} = \frac{\beta \pi}{m \omega}$.

In practice, the mass accelerated, initial velocity = 0, and the damping constant are determined as follows:

Determine an oscillation curve with the unknown mass. Determine a second oscillation curve by adding a 10 gram weight to the end of the transducer arm. Hence, $m_2 = m_1 + 10$.

The equations for the logarithmic decrements of the two curves are given by:

$$\ln y_1 - \ln y_2 = -\frac{\beta \pi}{2 m_1 \omega_1} \qquad (12.1)$$

$$\ln y_3 - \ln y_4 = -\frac{\beta \pi}{2(m_1 + 10)\omega_2} \qquad (12.2)$$

Dividing (12.1) by (12.2):

$$\frac{\ln (y_1 - y_2)}{\ln (y_3 - y_4)} = \frac{(m_1 + 10)\omega_2}{m_1 \omega_1}\ ; \quad m_1 \left[\frac{\ln(y_1 - y_2)}{\ln(y_3 - y_4)} \right] \omega_1 = (m_1 + 10)\omega_2 .$$

Hence, since the logs of the displacements and $\omega_1 + \omega_2$ are known, m_1 can be calculated. This done, the value of m_1 can be substituted back into equation (12.1), and β evaluated. Mass is measured in grams, ω = radians/sec = 2 π f where f = oscillations/sec, β = mass/time.

The given constant need not be calculated independently or experimentally, since:

$$\omega = \sqrt{\frac{k}{m} - \frac{\beta^2}{4 m^2}} \ .$$

Once m and β are known, k can be deduced.

The units of the quantities in the equation are as follows:

ω = radians/sec = 2 π f = frequency in cycles/sec = $\frac{1}{T}$

β = mass/time = grams/sec = $\frac{M}{T}$

k = mass/time^2 = grams/sec^2 = $\frac{M}{T^2}$.

A dimensional analysis of the terms in the above equation is as follows:

$$\omega = \sqrt{\frac{k}{m} - \frac{\beta^2}{4\,m^2}}$$

$$\frac{1}{T} = \sqrt{\frac{\frac{m}{T^2}}{m} - \frac{\frac{m^2}{T^2}}{m^2}}$$

$$\frac{1}{T} = \sqrt{\frac{1}{T^2} - \frac{1}{T^2}}$$

$$\frac{1}{T} = \frac{1}{T} \quad .$$

B. Experimental Examples

(a) An example of a calculation of the logarithmic decrement of a curve is as follows:

From the curve and data given on page 192-3 of Spiegel, Applied Differential Equations:

$y_n = 0.333$ inches

$y_{n+1} = 0.057$ inches

$\beta = 1.5$ lbs/sec

$m = \frac{6}{32}$ lbs.

$\omega = 4\sqrt{3}$ radians/sec

$$\frac{y_{n+1}}{y_n} = e^{-\frac{\beta \pi}{2 m \omega}}$$

$$\frac{0.0575}{0.333} = e^{-\frac{3.14 \cdot 1.5}{2 \cdot \frac{6}{32} \cdot 4\sqrt{3}}}$$

$$0.175 = e^{-1.73}$$

$$0.175 = 0.175$$

or, $$\ln \frac{y_n + 1}{y_n} = -\frac{\beta \pi}{2 m \omega} = -1.73$$

$$\ln 0.175 = -1.73$$

It may be that the oscillations will not be measured in radians/sec (ω). For example, suppose the time for one complete oscillation is measured, that is, the period. Then the frequency of the oscillation is $f = \frac{1}{T}$. Converting the frequency into ω units then, is

$$\omega = 2 \pi f = \frac{2 \pi}{T} .$$

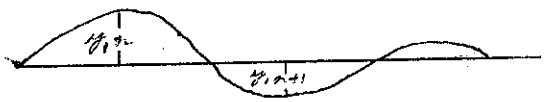
For example, the period of the example was 0.99 seconds. The frequency was therefore $\frac{1}{0.9\ \phi}$ or 1.01 cycles/sec, and

$$\omega = 2 \pi f = 2 \pi \cdot 1.61 = 6.928 = 4\sqrt{3} \text{ radians/sec.}$$

In practice, m is measured in grams by weighing on a balance, y is measured in cm, t in seconds, and k determined by adding weights to system and measuring displacement of system, calculated over a displacement of one cm. The weights used for the displacement are multiplied by 980 to give the constant the proper units: $\frac{M}{T^2}$, since $\frac{M}{L} \cdot \frac{L}{T^2} = \frac{M}{T^2}$.

(b) A check of calculation with single spring-mass system:

An oscillation curve is recorded from a single mass-spring arrangement  . A second curve is recorded after adding a 50 gram weight to the mass. The original mass and spring are weighed on a balance and found to be 325 grams. Hence, m = 325, m + 50 = 375.



m; f = 1.5 cps; $\omega = 2\pi f = 9.42$

$y_{1_n} = .250$ cm

$y_{1_n + 1} = .242$ cm

m + 50; f = 1.4 cps; $\omega = 2\pi f = 8.79$

$y_{2_n} = .250$ cm

$y_{2_n + 1} = .245$ cm

$$\frac{y_{1_n} + 1}{y_{1_n}} = e^{-\frac{\beta \pi}{2 m \omega}} \qquad \frac{y_{2_n} + 1}{y_{2_n}} = e^{-\frac{\beta \pi}{2 \omega (m + 50)}}$$

$$\ln\left(\frac{.242}{.250}\right) = -\frac{\beta \pi}{2 m\, 9.42} \qquad \ln\left(\frac{.245}{.250}\right) = -\frac{\beta \pi}{2 \cdot 8.79 (m + 50)}$$

$$\ln .9677\,(18.84\, m) = -\beta \pi \qquad \ln(.97)(17.58\, m + 879) = -\beta \pi$$

$$\ln .9677 = -.0328 \qquad \ln .97 = -.03046$$

$$-0.618\, m = -.536\, m - 26.81$$

$$.022\, m = 26.81$$

$$m = 325 \text{ grams}$$

$$m + 50 = 375 \text{ grams}$$

Note that the oscillation maximums must be measured with great accuracy.

β determination

$$-.0328 = -\frac{3.14\ \beta}{18.84 \cdot 325} \qquad -.03046 = -\frac{3.14\ \beta}{17.58 \cdot 375}$$

$$\beta = 63.7 \text{ grams/sec} \qquad \beta = 63.7 \text{ grams/sec}$$

The damping of the system is a force, and is equal here to 63.7 times the instantaneous velocity $\frac{dy}{dt}$. Hence, the damping force given numerically in grams equals 63.7 times $\frac{dy}{dt}$.

k determination

$$\omega = \sqrt{\frac{k}{m} - \frac{\beta^2}{4\ m^2}}$$

$\omega = 9.42$, $\beta = 63.7$, $m = 325$

$$k = \left(\omega^2 + \frac{\beta^2}{4\ m^2}\right) m = \left[(9.42)^2 + \frac{63.7^2}{4(325)^2}\right] 325$$

$= 28{,}800$ grams/sec^2. This is usually given simply as a constant, 28,800, meaning that a force of 28,800 dynes will deflect the spring/cm. In terms of masses hung on the spring, then

$\frac{28{,}800}{980} = 29.4$ grams will stretch the spring 1 cm.

Experimentally, a 50 gram weight hung on the spring deflected the spring 1.7 cm. Hence 29.4 grams deflected the spring 1 cm, or a force of 29.4 x 980 = 28,800 dynes.

(c) Another example, determined on actual recording systems:

The natural frequency of strain gage arm is about 140 cps. The strain gage amplifier output is linear only up to 40 cps. Hence, 5.94 grams added to end of strain gage arm to reduce natural frequency.

Let m_x = mass of strain gage arm set in motion by displacing arm from equilibrium position, and then releasing; effective mass of arm alone.

$m_1 = m_x + 5.94$ grams.

$m_2 = m_x + 5.94 + 1.59$ grams; $m_1 + 1.59$ grams.

Two oscillation curves are measured from the system. One with mass m_1, the other with mass m_2.

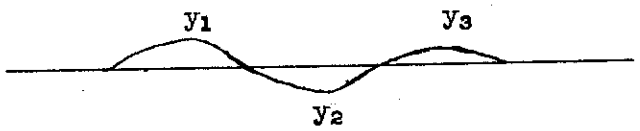
From m_1 curve

frequency = 29.1 cps; $\omega_1 = 2\pi f = 182.4$.

From m_2 curve

frequency = 24.8 cps; $\omega_2 = 156$.

The logarithmic decrement of both curves the same: $\frac{y_3}{y_1} = 0.979$.



Hence,

$$0.979 = e^{-\frac{\beta \pi}{m_1 \omega_1}} \qquad 0.979 = e^{-\frac{\beta \pi}{m_2 \omega_2}}$$

and, $$\omega_1 m_1 = \omega_2 m_2$$

$$182.4\ m_1 = 156\ m_1 + 248.14$$

$$m_1 = 9.42 \text{ grams.}$$

Hence, $$m_x = 3.48 \text{ grams}$$

Effective mass of strain gage arm = 3.48 grams.

From the relation:

$$\frac{y_3}{y_1} = e^{-\frac{\beta \pi}{m_1 \omega_1}} = 0.979 = e^{-\alpha}.$$

From e^{-x} tables, $\alpha = 0.021$,

hence,

$$\beta = \frac{(0.021)(9.42)(182.4)}{3.1416}.$$

β = 11.16 grams per sec.; damping coefficient.

From the relation:

$$\omega_1 = \sqrt{\frac{k_1}{m_1} - \frac{\beta^2}{4m_1^2}}$$

$$182.4 = \sqrt{\frac{k}{9.42} - \frac{(11.16)^2}{4(9.42)^2}}$$

$$33{,}271 = \frac{k}{9.42} - \frac{124.5}{355}$$

$$k = (33{,}271 + .35)\ 9.42$$

k = 313,413 grams per sec.^{2}

Hence = $\frac{313,413}{980}$ = 320 grams will deflect the strain gage arm 1 cm.

Experimental verification of k:

End of strain gage arm observed under microscope. Found that 1 gram added to arm deflects arm 0.0029988 cm. Hence, 334 grams will deflect arm 1 cm.

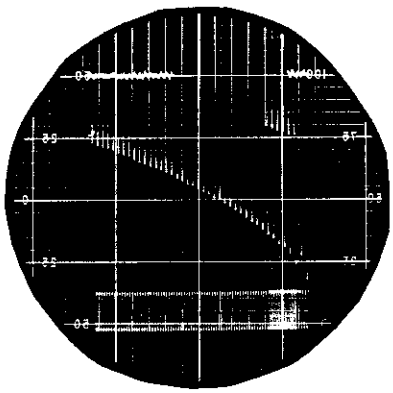
Difference between calculated and experimental k values = $\frac{334 - 320}{320}$ = 4.4%.

DATA OF EXAMPLE C

M_1

y = base line = 100

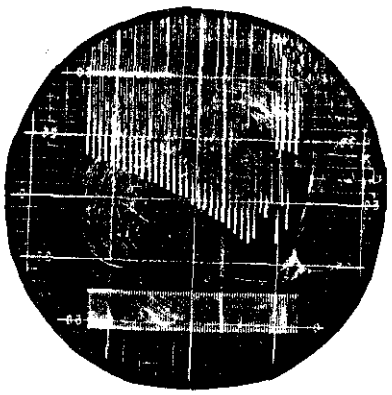
y, Number of Oscillations	Amplitude, mm.
1	21.5
2	21.0
3	20.3
4	19.8
5	19.2
6	18.7
7	18.1
8	17.7
9	17.3
10	16.9
11	16.3
12	15.75
13	15.35
14	14.95
15	14.55
16	14.35
17	13.85
18	13.55
19	13.05
20	12.75

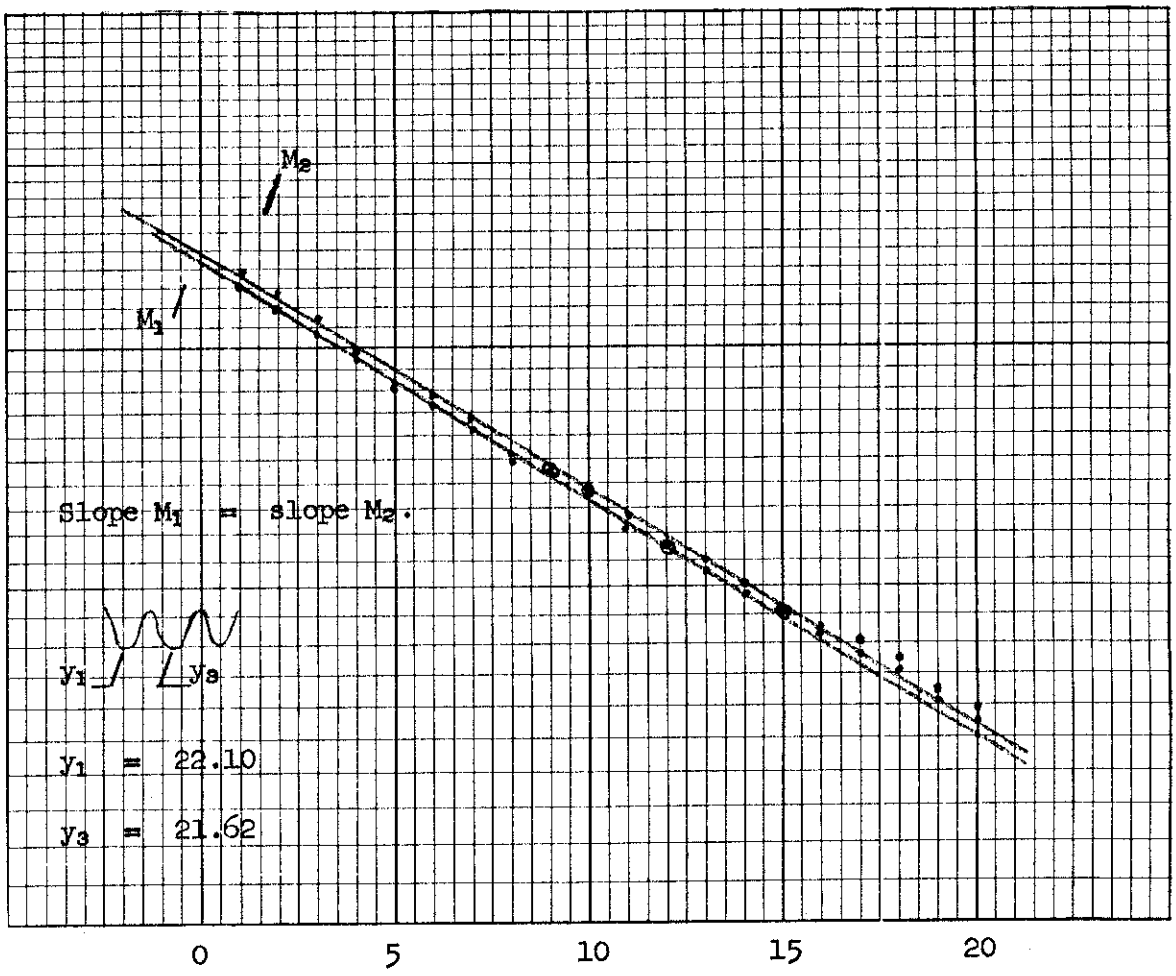


M_2

y = base line = 100

y, Number of Oscillations	Amplitude, mm.
1	21.8
2	21.3
3	20.6
4	19.8
5	19.1
6	18.8
7	18.2
8	17.5
9	17.3
10	16.90
11	16.05
12	15.75
13	15.55
14	15.05
15	14.65
16	14.25
17	14.05
18	13.75
19	13.05
20	12.95




M2
M1
Slope M1 = slope M2.
y1
y3
y1 = 22.10
y3 = 21.62
0
5
10
15
20

CHAPTER 13

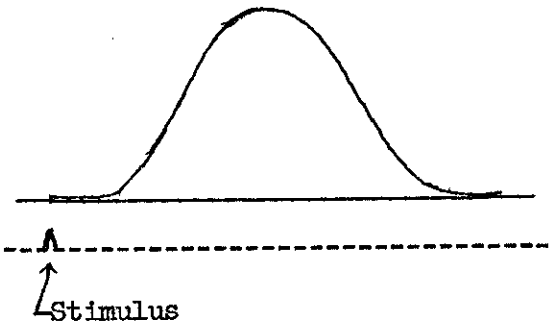
DETAILED PROCEDURE FOR ANALYSIS OF MUSCLE TWITCH CURVES, PART I

This and the following chapter describe the detailed procedure for the experimental analysis of a twitch curve. A twitch of a rat heart column is used as the illustrative material.

A. Recording Procedure

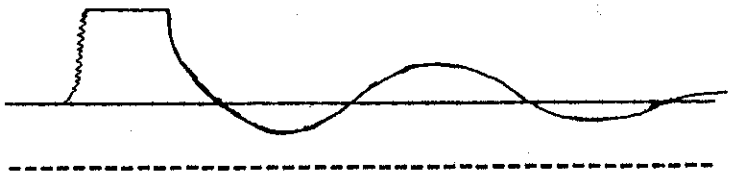
(a) Equilibrate muscle column for 30 minutes; stimulated at rate of 6/minute; under one gram resting tension; Ringer's solution circulating and oxygenated; fluid level just at top of muscle. Measure muscle length, width, and length from bottom of muscle to point on or on top of strain gage box.

(b) Record twitch curve at 30 minute mark, from t = 0, on oscilloscope, with time and base line:

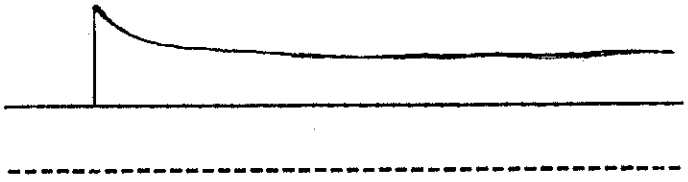


(c) Record damping curve, between twitches; displace strain gage arm upward and release; record on oscilloscope or recorder, with

time and base line:



(d) Determine stiffness coefficient: shut off stimulator, and with micrometer, displace gage box upward, record on recorder to equilibrium; measure new system length.

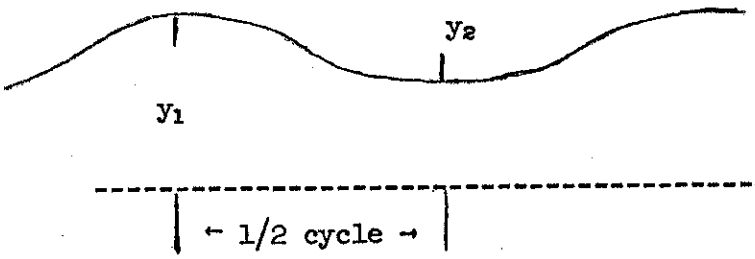


(e) Remove free portion of muscle, dry and weigh.

B. Analysis Procedure

(a) M = mass of muscle + effective mass of gage + connecting arm mass. Consider muscle mass negligible. Strain gage effective mass 3.48 grams.

(b) R = damping constant, from damping curve:



1. Measure distance y_1 in cm.
2. Measure distance y_2 in cm.
3. Measure time for 1/2 cycle in seconds = 1/2 f, using 60 cycle signal; each wave = 1/60 second.
4. 2 x 1/2 f = f cps.
5. Multiply f by 2π = ω.
6. Substitute y_1, y_2, M, π and ω into

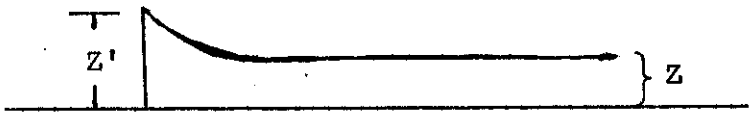
$$\frac{y_2}{y_1} = e^{-\frac{R\pi}{2 M \omega}} = e^{-\frac{\alpha}{\omega}} .$$

7. From e^{-x} tables, find value of x so that

$$e^{-x} = \frac{y_2}{y_1} .$$

8. $R = \frac{2 M \omega x}{\pi}$, grams/second.

(c) $\underline{K}$ = stiffness coefficient, taken from stiffness curve:



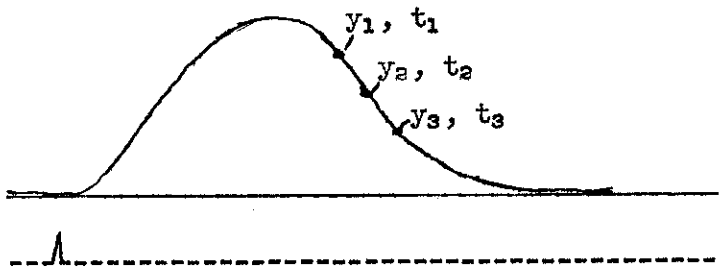
1. Measure initial system length in cm, x_1.
2. Measure displaced system length in cm, x_2.
3. $\Delta x = x_2 - x_1$, cm.
4. From calibration chart, measure Z in grams.
5. Multiply Z by 980 to give F.
6. Then

$$K, \text{ grams/sec}^2 = \frac{F, \text{ grams cm x sec}^{-2}}{\Delta x, \text{ cm.}}$$

7. Check by substituting ω,M, and R into

$$K = M\left(\omega^2 + \frac{R^2}{4M^2}\right).$$

(d) k_2 = second rate constant



1. From twitch curve, measure three points, convert measurements into cm displacement of system.
2. Measure corresponding times in seconds from t = 0, peak of stimulus curve.
3. Calculate k_2 from:

$$k_2 = \frac{\ell n \left[\frac{-C \pm \sqrt{C^2 + 4DE}}{2D} \right]}{t_3 - t_2}$$

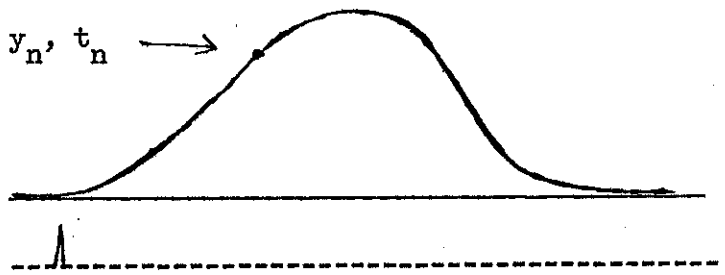
where

$$C = y_3 e^{-\frac{Rt_1}{2M}} - y_1 e^{-\frac{Rt_3}{2M}}$$

$$D = y_2 e^{-\frac{Rt_3}{2M}} - y_3 e^{-\frac{Rt_2}{2M}}$$

$$E = y_2 e^{-\frac{Rt_1}{2M}} - y_1 e^{-\frac{Rt_2}{2M}}$$

(e) $\underline{k_1}$ = first rate constant



1. Measure any point on twitch curve, y_n, t_n, convert into cm displacement and seconds time.

2. With y_1, t_1, y_2, t_2 from calculation of k_2, calculate k_1 from

$$k_1 = \frac{\ln\left[\dfrac{y_n + Ze^{-k_2 t_n} + (\omega - Z)\, e^{-\frac{R\, t_n}{2M}}}{\omega}\right]}{t_n}$$

where

$$Z = \frac{y_1 e^{-\frac{Rt_2}{2M}} - y_2 e^{-\frac{Rt_1}{2M}}}{e^{-(k_2 t_2 + \frac{Rt_1}{2M})} - e^{-(k_2 t_1 + \frac{Rt_2}{2M})}}$$

$$W = \frac{y_1 e^{-k_2 t_2} - y_2 e^{-k_2 t_1}}{e^{-(k_2 t_1 + \frac{Rt_2}{2M})} - e^{-(k_2 t_2 + \frac{Rt_1}{2M})}} + \frac{y_1 e^{-\frac{Rt_2}{2M}} - y_2 e^{-\frac{Rt_1}{2M}}}{e^{-(k_2 t_2 + \frac{Rt_1}{2M})} - e^{-(k_2 t_1 + \frac{Rt_2}{2M})}}$$

NOTE: The methods for determining k_1 and k_2 are unproven and perhaps questionable.

(f) $\underline{pA_0}$ = proportionality constant and initial amount of A substance.

From previous calculations:

$$pA_0 = \frac{Z(k_2^2 - \frac{R}{M} k_2 + \frac{K}{M})(Mk_2 - Mk_1)}{k_1} .$$

C. Programing of Computer

Basic equation:

$$\frac{d^2y}{dt^2} + \frac{R}{M}\frac{dy}{dt} + \frac{K}{M}y = \frac{pA_0\ k_1}{M(k_2 - k_1)}\left(e^{-k_1 t} - e^{-k_2 t}\right).$$

Since $k_1 > k_2$, right hand side of the equation is negative, and since

$$\frac{pA_0\ k_1}{k_2 - k_1}\left(e^{-k_1 t} - e^{-k_2 t}\right) = \frac{pA_0\ k_1}{k_1 - k_2}\left(e^{-k_2 t} - e^{-k_1 t}\right),$$

the right hand side being positive, write basic equation as

$$\frac{d^2y}{dt^2} + \frac{R}{M}\frac{dy}{dt} + \frac{K}{M}y = pA_0\left[\frac{k_1}{M(k_1 - k_2)}\right]\left(e^{-k_2 t} - e^{-k_1 t}\right).$$

Use this equation for programing.

Time Scaling

A muscle contraction requires about 0.2 seconds per twitch, or the frequency of the motion is about 5 cps. When recording on a Sanborn or scope, this is not too fast so time scaling need not be done. Computer amplifier phase shift is only 0.5° at 1000 cps, so this is not limiting either.

If time scaling is decided upon, it is done as follows:

The natural undamped frequency is determined:

$$\omega_n = \sqrt{\frac{K}{M}} \; ; \; f = \frac{\omega}{2\pi} = \frac{1}{2\pi}\sqrt{\frac{K}{M}}$$

$$\left[\begin{array}{l} \text{If } f = 5 \text{ cps, } M = 5 \text{ grams; } 5 = \frac{1}{6.28}\sqrt{\frac{K}{5}} \\ K = 4{,}929.8 \text{ grams/sec}^2. \end{array}\right]$$

Suppose $\omega_n = 31.40$ radians/sec, and it is decided to slow computer solution to 3.14 radians/sec. Here, twitch takes 10 times as long to complete, or 2 seconds. Hence, for every time t in equation, replace with $10t = \tau$; $t = \frac{\tau}{10}$.

Thus:

$$t = \frac{\tau}{10}, \quad \frac{dy}{dt} = \frac{dy}{d\frac{\tau}{10}} = 10\frac{dy}{d\tau}; \quad \frac{d^2y}{dt^2} = \frac{d^2y}{d(\frac{\tau}{10})^2} = 100\frac{d^2y}{d\tau^2}.$$

Making the substitutions into the equation

$$\frac{d^2y}{dt^2} + \frac{R}{M}\frac{dy}{dt} + \frac{K}{M}y = pA_o\left[\frac{k_1}{M(k_1 - k_2)}\right](e^{-k_2 t} - e^{-k_1 t})$$

$$100\frac{d^2y}{d\tau^2} + 10\frac{R}{M}\frac{dy}{d\tau} + \frac{K}{M}y = pA_o\left[\frac{k_1}{M(k_1 - k_2)}\right](e^{-.1k_2\tau} - e^{-.1k_1\tau})$$

In matching real twitch curves with scaled computer curves, if computer solution is slowed 10 times, then oscilloscope sweep rate is reduced ten times that used to record actual muscle twitch:

Recorded twitch

Scope speed: 1/sec.

Matched computer solution, scaled $t = \frac{\tau}{10}$

Scope speed: 1/10 sec.

Note on initial conditions and time scaling:

If at $t = 0 \quad y = 0, \quad \frac{dy}{dt} = 0, \quad \frac{d^2y}{dt^2} = 0$,

then at $\tau = 0 \quad y = 0, \quad \frac{dy}{d\tau} = 0, \quad \frac{d^2y}{d\tau^2} = 0$;

but if at $t = 0, \quad y = 0, \quad \frac{dy}{dt} = 5, \quad \frac{d^2y}{dt^2} = 10$,

then at $\tau = 0, \quad y = 0,$ and since $\frac{dy}{dt} = 10\,\frac{dy}{d\tau} = 5, \quad \frac{dy}{d\tau} = .5$,

likewise $\frac{d^2y}{d\tau^2} = \frac{10}{100} = .1$.

For problem under discussion, assume at

$$t = 0, \quad y = 0, \quad \frac{dy}{dt} \neq \frac{d^2y}{dt^2} = 0 .$$

CHAPTER 24

DETAILED PROCEDURE FOR ANALYSIS OF MUSCLE TWITCH CURVES, PART II

A. Amplitude Scaling

The magnitude of the equation variables are estimated as follows: (Remember, keep all voltage outputs of amplifiers away from zero and between ± 100 volts.)

Estimate the magnitude of maximum shortening y directly.

Example: Maximum tension is found to be 200 mg/mm equilibrium length, and the equilibrium length is 10 mm. Hence, maximum tension = 2 grams. If 1 gram deflects gage arm .003 cm, then 2 grams = .006 cm deflection. Therefore y_{max} = .006 cm.

Estimate magnitude of derivatives from consideration of natural undamped frequency: if ω_n = 30 radians/sec.

$$\frac{dy}{dt}_{max} = 30 \times y_{max} = 0.18 \text{ cm/sec.}$$

$$\frac{d^2y}{dt^2}_{max} = 30^2 \times y_{max} = 5.4 \text{ cm/sec}^2.$$

Set

1 volt = 1 cm shortening

1 volt = 1 cm/sec velocity

1 volt = 1 cm/sec^2 acceleration.

The maximum outputs of the respective amplifiers should then be, after multiplying terms by an arbitrary amount to give output voltages in 50 volt range:

$$y_{max} \times (10{,}000) = 6 \times 10^{-3} \times 10{,}000 = 60 \text{ volts}$$

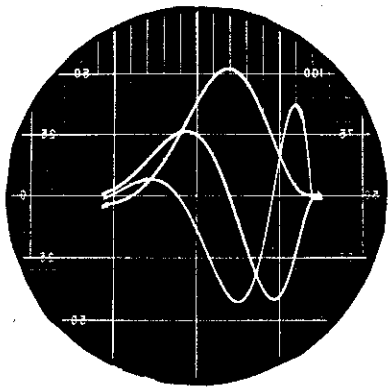
$$\left(\frac{dy}{dt}\right)_{max} \times (300) = 180 \times 10^{-3} \times 300 = 54 \text{ volts}$$

$$\left(\frac{d^2y}{dt^2}\right)_{max} \times (10) = 5{,}400 \times 10^{-3} \times 10 = 54 \text{ volts.}$$

Estimate the maximum value of $pA_0 \left[\frac{k_1}{M(k_1 - k_2)}\right] (e^{-k^2 t} - e^{-k_1 t})$ as follows:

This term must be equal to (i.e., the maximum value of the term) the maximum value of the left hand side of the basic equation.

Below is a record of an equation solved by the computer, simultaneously recording y, $\frac{dy}{dt}$, and $\frac{d^2y}{dt^2}$:



$y = + \uparrow$

$\dot{y} = + \downarrow$

$\ddot{y} = + \uparrow$

$\leftarrow t$

Observation of the curves shows that when y = max, $\frac{dy}{dt} = 0$; when $\frac{dy}{dt}$ = max, $\frac{d^2y}{dt^2} = 0$; and when $\frac{d^2y}{dt^2}$ = max, $\frac{dy}{dt} \cong 50\%$ of max, and $y \cong 10\%$ max.

$\therefore$ for maximum value of left hand side of equation, take

$$\left(\frac{d^2y}{dt^2}\right)_{max} + \frac{1}{2}\left(\frac{dy}{dt}\right)_{max} + \frac{1}{10}\,y_{max} = \text{total maximum of forcing function.}$$

This is equal to $5{,}400 \times 10^{-3} + 90 \times 10^{-3} + .6 \times 10^{-3}$

$$= 5{,}500 \times 10^{-3}.$$

Let 1 volt = 1 unit of the forcing term.

The amplifier output should therefore be, multiplying by an arbitrary value:

$$pA_0 \left[\frac{k_1}{M(k_1 - k_2)}\right](e^{-k_2 t} - e^{-k_1 t}) \times (10) = 5{,}500 \times 10^{-3} \times (10) = 55 \text{ volts.}$$

Now consider the basic equation:

$$\frac{d^2y}{dt^2} + \frac{R}{M}\frac{dy}{dt} + \frac{K}{M}y = pA_0 \left[\frac{k_1}{M(k_1 - k_2)}\right](e^{-k_2 t} - e^{-k_1 t}).$$

Substituting into the equation the values for the constant terms:

R	= 90	$(e^{-k_2 t} - e^{-k_1 t})$	$\cong .1$
M	= 5		
K	= 50,000	$\frac{k_1}{M(k_1 - k_2)}$	= 5
k_1	= 25		
k_2	= 24	pA_0	$\cong 26$

pA_o is determined to be approximately 26, since the maximum value of the entire forcing term is approximately:

$$5{,}400 \times 10^{-3} + 18 \cdot 90 \times 10^{-3} + 10{,}000 \cdot .6 \times 10^{-3} = 13 .$$

Hence,

$$.5\ pA_o \cong 13, \quad pA_o \cong 26 .$$

Substituting these values into the equation gives:

$$\frac{d^2y}{dt^2} + 18\frac{dy}{dt} + 10{,}000\ y = 130\ (e^{-24t} - e^{-25t}) .$$

However, this gives the natural frequency of:

$$\omega_n = \sqrt{10{,}000} = 100 \text{ radians/sec.}$$

But $\omega_n \cong 30$ radians/sec; therefore K is probably too large, at first glance. The actual frequency is:

$$\omega = \sqrt{\frac{K}{M} - \frac{R^2}{4M^2}} = 99 \text{ radians/sec.}$$

Therefore, reduce K to 5,000, giving an actual frequency of:

$$\omega_A = \sqrt{\frac{5{,}000}{5}} - 81 = 30 + \text{ radians/sec.}$$

This will change the value of pA_o to:

$$5{,}400 \times 10^{-3} + 18 \cdot 90 \times 10^{-3} + 1{,}000 \cdot .6 \times 10^{-3} \cong 8$$

$$.5\ pA_o \cong 8, \quad pA_o \cong 16 .$$

The equation becomes:

$$\frac{d^2y}{dt^2} + 18\frac{dy}{dt} + 1{,}000\,y = 80\,(e^{-24t} - e^{-25t}) .$$

Again, letting 1 volt = 1 cm y, 1 cm/sec $\dot{y}$, 1 cm/sec^2 $\ddot{y}$ and considering the recommended multiplication of the variables for adequate voltage outputs:

$y \times (10{,}000)$

$\dot{y} \times (300)$

$\ddot{y} \times (10)$

$f(t) \times (10)$

It becomes apparent that multiplying the equation by 10 will give:

$$10\frac{d^2y}{dt^2} + 180\frac{dy}{dt} + 10{,}000\,y = 800(e^{-24t} - e^{-25t}) .$$

The maximum voltages expected from the variable terms would now be:

$$10\frac{d^2y}{dt^2} = 10 \times 5{,}400 \times 10^{-3} = 54 \text{ volts}$$

$$180\frac{dy}{dt} = 180 \times 180 \times 10^{-3} = 32.4 \text{ volts}$$

$$10{,}000\,y = 10{,}000 \times 6 \times 10^{-3} = 60 \text{ volts}$$

$$800(e^{-24t} - e^{-25t}) = 800 \times .1 = 80 \text{ volts.}$$

Hence, scaling the equation by a factor of 10 yields acceptable outputs for all terms.

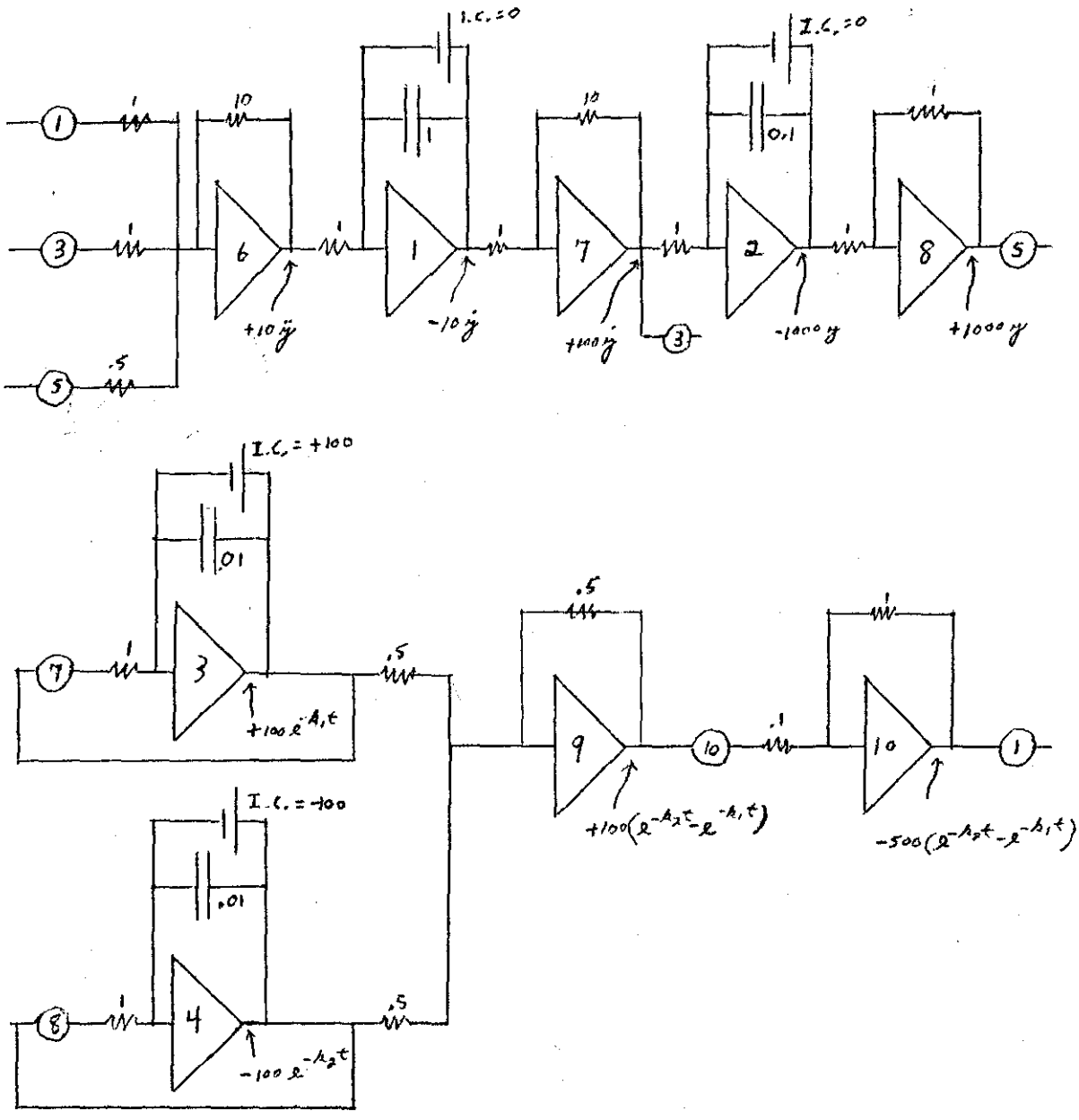
The scaled equation is programed for the computer as follows:

Putting the equation in the form:

$$10\,\ddot{y} = 800(e^{-24t} - e^{-25t}) - 180\,\dot{y} - 10{,}000\,y\ .$$

B. Computer Circuit Diagram

The circuit diagram for the computer setup is:



Calculation of resistor, capacitor, and potentiometer values for circuit diagram follows.

General Formulae

(a) Summing amplifier:

$$e_o = - R_F \left(\frac{a_1 e_1}{R_1} + \frac{a_2 e_2}{R_2} \ldots \right).$$

(b) Integrating amplifier:

$$e_o = - \frac{1}{C_F} \left(\frac{a_1}{R_1} \int e_1 dt + \frac{a_2}{R_2} \int e_2 dt \ldots \right).$$

Amplifier 1

Desired Output $= - 10 \dot{y}$

Input $= + 10 \ddot{y}$

$$e_o = - \frac{1}{C_F} \left(\frac{a}{R} \int e_1 dt \right)$$

Thus: $C_F = 1$

$R = 1$

$$- 10 \dot{y} = - \frac{1}{1} \left(\frac{1}{1} \int 10 \ddot{y} \, dt \right)$$

Coefficient $= 10$

$$= - \int 10 \ddot{y} \, dt = - 10 \dot{y}$$

Amplifier 2

Desired Output $= - 1000 y$

Coefficient $= 1000$

Input $= + 100 \dot{y}$

$$- 1000 y = - \frac{1}{0.1} \left(\frac{1}{1} \int 100 \dot{y} \, dt \right)$$

Thus: $C_F = 0.1$

$R = 1$

$$= - 1000 y$$

Amplifier 3, Potentiometer (7)

Desired Output $= + 100\, e^{-k_1 t}$

Input $= + 100\, e^{-k_1 t}$ where $k_1 = 25$

$e_o = -\frac{1}{C_F}\left(\frac{a}{R}\int e_1\, dt\right)$ Coefficient $= 100\, k_1$

$100\, e^{-k_1 t} = -\frac{1}{.01}\left(\frac{a}{1}\int 100\, e^{-k_1 t}\, dt\right)$

$= -\frac{100\, a}{.01}\left(-\frac{e^{-k_1 t}}{k_1}\right)$

$= \left(100\, e^{-k_1 t}\right)\left(\frac{a}{.01\, k_1}\right)$; Let $a = .25$

$100\, e^{-k_1 t} = \left(100\, e^{-k_1 t}\right)\left(\frac{.25}{.25}\right)$ Thus: $C_F = .01$,

$R = 1$,

$a = .25$.

Amplifier 4, Potentiometer (8)

As in amplifier 3, $k_2 = 24$

$-100\, e^{-k_2 t} = -100\, e^{-k_2 t}\left(\frac{a}{.01\, k_2}\right)$, Let $a = .24$

Thus: $C_F = .01$, $R = 1$, $a = .24$ Coefficient $= 100\, k_2$

Amplifier 6, Potentiometer ①, ③, and ⑤

$$\text{Desired Outputs} = -800(e^{-k_2 t} - e^{-k_1 t}) + 180\,\dot{y} + 10{,}000\,y$$

$$\text{Inputs} = -500(e^{-k_2 t} - e^{-k_1 t}) + 100\,\dot{y} + 1000\,y$$

Consider above before going through amplifier, hence no sign change, and then treat separately.

① $e_o = R_F\left(\frac{a_1 e_1}{R_1}\right)$ Coefficient = $(10)\overset{16}{\#} pA_o \left[\frac{\overset{5}{\#} k_1}{M(k_1 - k_2)}\right]$

$$-800(e^{-k_2 t} - e^{-k_1 t}) = 10\left(\frac{a_1[500(e^{-k_2 t} - e^{-k_1 t})]}{1}\right)$$

$a_1 = 0.16$ $R_F = 10$, $R_1 = 1$.

③ $180\,\dot{y} = 10\left(\frac{a_2 \cdot 100\,\dot{y}}{1}\right)$ Coefficient = $(10)\overset{18}{\#}\frac{R}{M}$

$a_2 = 0.18$ $R_F = 10$, $R_1 = 1$

⑤ $10{,}000\,y = 10\left(\frac{a_3 \cdot 1000\,y}{.5}\right)$ Coefficient = $10\left(\frac{\overset{1{,}000}{\#} K}{M}\right)$

$a_3 = 0.5$ $R_F = 10$, $R_1 = .5$

Considered together:

$$\text{desired output} = +10\,\ddot{y} = 800(e^{-k_2 t} - e^{-k_1 t}) - 180\,\dot{y} - 10{,}000\,y$$

$$e_o = -R_F\left(\frac{a_1 e_1}{R_1} + \frac{a_2 e_2}{R_2} + \frac{a_3 e_3}{R_3}\right)$$

$$+10\,\ddot{y} = -10\left(-\frac{(.16)(500)(e^{-k_2 t} - e^{-k_1 t})}{1} + \frac{(.18)(100\,\dot{y})}{1} + \frac{(.5)(1000\,y)}{.5}\right)$$

Amplifier 7

Desired Output $= +100\,\dot{y}$ Coefficient = (100)

Input $= -10\,\dot{y}$

$$e_o = -R_F\left(\frac{a_1 e_1}{R_1}\right)$$

$$+100\,\dot{y} = -10\left(\frac{1 \cdot (-10\,\dot{y})}{1}\right) = +100\,\dot{y} \qquad R_F = 10,\ R_1 = 1$$

Amplifier 8

Desired Output $= +1000\,y$ Coefficient = 1000

Input $= -1000\,y$ $R_F = 1,\ R_1 = 1$

Amplifier 9

Desired Output $= +100\,(e^{-k_2 t} - e^{-k_1 t})$

Inputs $= +100\,e^{-k_1 t} + (-100\,e^{-k_2 t})$

$R_F = .5,\ R_1 + R_2 = .5$ Coefficient = (100)

Amplifier 10, Potentiometer (10)

Desired Output $= -500\,(e^{-k_2 t} - e^{-k_1 t})$

Input $= +100\,(e^{-k_2 t} - e^{-k_1 t})$

$$-500(e^{-k_2 t} - e^{-k_1 t}) = -1\left(\frac{(a)\,100\,(e^{-k_2 t} - e^{-k_1 t})}{.1}\right)$$

$a = .5$ $\quad R_F = 1,\ R_1 = .1$ $\quad$ Coefficient $= (100)\,\frac{k_1}{M(k_1 - k_2)}$ $\quad$ 5

Note on Scaling:

If no scaling, and 1 volt = 1 cm y, and

if output of y amp. = 1,000 y = 6 volts, then

$$y = \frac{6}{1{,}000} = .006 \text{ cm.}$$

If equation is scaled by 10, then output = 10,000 y = 60 volts,

$$y = \frac{60}{10{,}000} = .006 \text{ cm.}$$

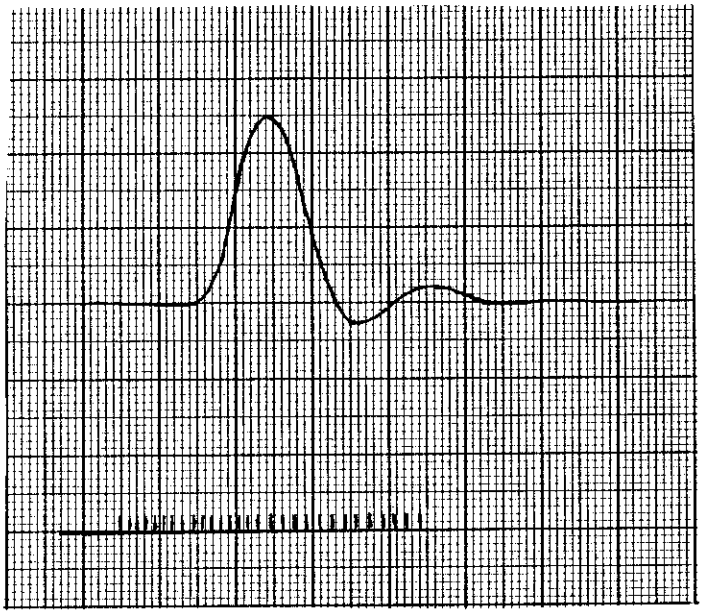
In summary, potentiometer equivalences:

Pot.	Term	Actual Term Values	Pot. Setting, a	Equivalent
①	pA_o	16	.16	$a_1 = .01\ pA_o$; $pA_o = 100\ a_1$
③	$\frac{R}{M}$	18	.18	$a_3 = .01\ \frac{R}{M}$; $\frac{R}{M} = 100\ a_3$
⑤	$\frac{K}{M}$	1,000	.5	$a_5 = .0005\ \frac{K}{M}$; $\frac{K}{M} = 2{,}000\ a_5$
⑦	k_1	25	.25	$a_7 = .01\ k_1$; $k_1 = 100\ a_7$
⑧	k_2	24	.24	$a_8 = .01\ k_2$; $k_2 = 100\ a_8$
⑩	$\frac{k_1}{M(k_2 - k_1)}$	5	.5	$a_{10} = \frac{1}{10}\ \frac{k_1}{M(k_2 - k_1)}$; $\frac{k_1}{M(k_2 - k_1)} = 10\ a_{10}$

If a curve is matched by setting ① = .35, ③ = .26, and ⑦ = .21, then $pA_o = 100 \cdot .35 = 35$; $\frac{K}{M} = 2{,}000 \cdot .26 = 520$ ($K = 520 \times 5 = 2600$); $k_1 = 100 \cdot .21 = 21$.

These experimental pot. settings are <u>not</u> read off the dial, but measured from the reference voltage.

The following is a computer solution of the equation as programed, with 60 cycle timing.



Actual Pot Settings:

① = .163	⑦ = .259
③ = .185	⑧ = .248
⑤ = .525	⑩ = .558

CHAPTER 25

ANALYSIS OF RESTING BEHAVIOR OF MUSCLE; ELECTRICAL CIRCUITS

In the analysis of mechanical models set up to describe muscle behavior, it is often simplest to construct analogous electrical circuits, and to describe their "behavior" through differential equations. Such equations are identical to those describing the mechanical models. The analysis of circuits is performed as follows:

A. General Principles

1. The voltage drop across a resistor is proportional to the current passing through the resistor:

$$E_R = RI$$

2. The voltage drop across an inductor is proportional to the instantaneous time rate of change of the current:

$$E_L = L \frac{dI}{dt},$$

where L = constant of proportionality or coefficient of inductance, or simply inductance.

The inductance has inertia effects, opposing a change in current; this is similar to a mass having inertia effects in mechanics, which opposes a change in motion or velocity.

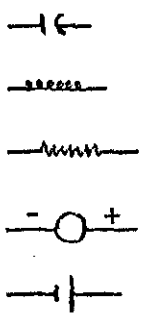
3. The voltage drop across a capacitor is proportional to the instantaneous electric charge on the capacitor:

$$E_C = \frac{Q}{C},$$

where Q is the instantaneous charge, $\frac{1}{c}$ is the constant of proportionality of capacitance, or simply capacitance. Also, since

$$I = \frac{dQ}{dt}, \quad Q = \int I dt .$$

4. Symbols to be used:



Capacitor

Inductor

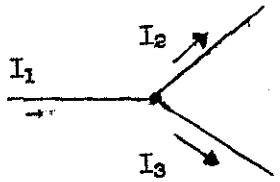
Resistor

Generator or

Battery

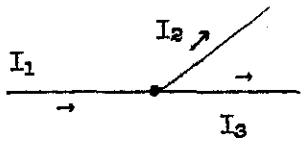
5. The algebraic sum of all voltage drops around an electric loop or circuit is zero; or, the voltage supplied (e m f) to a circuit is equal to the sum of the voltage drops in the circuit. This is Kirchhoff's second law.

6. The algebraic sum of the currents travelling toward and away from branch points in a circuit is equal to zero. This is Kirchhoff's first law.



$$I_1 = I_2 + I_3, \; I_1 + I_2 + I_3 = 0 .$$

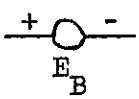
7. If I is + in one direction, it is negative in the opposite direction, the direction taken from a point:



I_1 = +, I_2, I_3 = −

8. The potential drop across an element is + if the analysis proceeds in the same direction as the current flow; - if in the opposite direction.

9. A potential rise in a circuit, due to a battery or generator, is considered to be the negative of a potential drop:

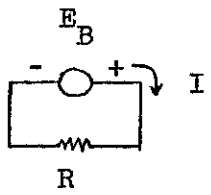


Direction of Analysis →

Consider in this analysis, that there is a potential drop, + to -, across the battery. Hence, E_B is taken as +. If the analysis were to proceed counterclockwise, from - to +, then E_B would be taken as -.

B. Examples of Analysis

1. Battery + Resistor



Analysis = Clockwise

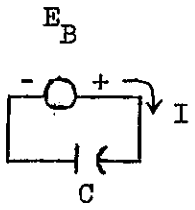
From A8 and A1: $E_R = +RI = +R\frac{dQ}{dt}$

From A9: $E_B = -E_B$

From A5: $-E_B + R\frac{dQ}{dt} = 0$; $E_B = R\frac{dQ}{dt}$

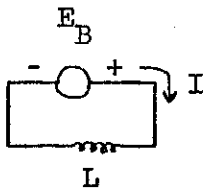
$E_B = R\frac{dQ}{dt}$

2. Battery + Capacitor



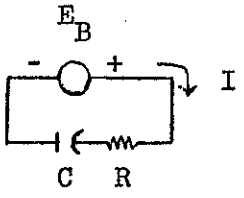
$E_B = \frac{1}{C}Q$

3. Battery + Inductor



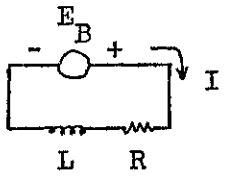
$E_B = L\frac{dI}{dt} = L\frac{d^2Q}{dt^2}$

4. Battery + Resistor + Capacitor



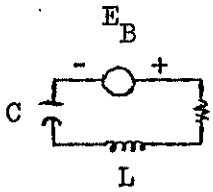
$E_B = R\frac{dQ}{dt} + \frac{1}{C}Q$

5. Battery + Resistor + Inductor



$$E_B = L\frac{d^2Q}{dt^2} + R\frac{dQ}{dt}$$

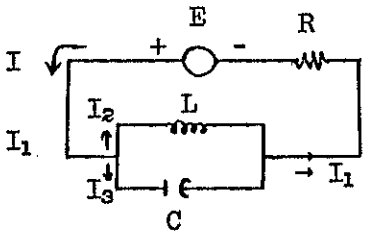
6. Battery + Resistor + Capacitor + Inductor



$$E_B = L\frac{d^2Q}{dt^2} + R\frac{dQ}{dt} + \frac{1}{C}Q$$

The equation for this circuit is completely analogous to that for a damped, oscillatory motion.

7. Divided circuit:



In this circuit there are three closed loops, and accordingly, three equations for their description. The closed loops are: battery + resistor + inductance; battery + resistor + capacitance; inductance + capacitance.

Analysing the first loop, clockwise:

$$E_B = +E,\ E_R = -R\frac{dQ_1}{dt},\ E_L = -L\frac{d^2Q_2}{dt^2} \qquad \left[\ RI_1 = R\frac{dQ_1}{dt}\ \right].$$

Hence:

$$E = L\frac{d^2Q_2}{dt^2} + R\frac{dQ_1}{dt}\ .$$

In the second loop:

$$E_B = +E,\ E_R = -R\frac{dQ_1}{dt},\ E_c = -\frac{1}{C}Q_3 \qquad \left[Q_3 \text{ proportional to } I_3\right].$$

Hence:

$$E = R\frac{dQ_1}{dt} + \frac{1}{C}Q_3\ .$$

In the third loop, clockwise again:

$$E_L = L\frac{d^2Q_2}{dt^2};\quad E_c = -\frac{1}{C}Q_3\ .$$

Hence:

$$0 = L\frac{d^2Q_2}{dt^2} - \frac{1}{C}Q_3\ .$$

Therefore, the three equations are:

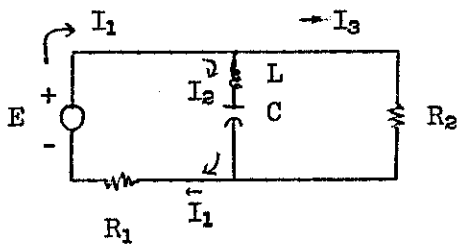
$$E = L\frac{d^2Q_2}{dt^2} + R\frac{dQ_1}{dt} \qquad (1)$$

$$E = R\frac{dQ_1}{dt} + \frac{1}{C}Q_3 \qquad (2)$$

$$0 = L\frac{d^2Q_2}{dt^2} - \frac{1}{C}Q_3 \qquad (3)$$

In these three equations, notice that (3) is obtained by subtracting (2) from (1). In principle, such divided circuits need be analized only for two equations. The third, representing the loop without the battery, can always be obtained from the other two.

8. Another divided circuit:



3 loops present

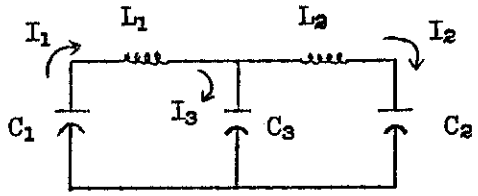
Analysing clockwise:

$$E = L\frac{d^2Q_2}{dt^2} + R_1\frac{dQ_1}{dt} + \frac{Q_2}{C}$$

$$E = R_2\frac{dQ_3}{dt} + R_1\frac{dQ_1}{dt}$$

$$0 = -L\frac{d^2Q_2}{dt^2} + R_2\frac{dQ_3}{dt}$$

9. Another divided circuit:



Analyzing clockwise, the equations are:

$$L_1 \frac{d^2Q_1}{dt^2} + \frac{1}{C_3} Q_3 + \frac{1}{C_1} Q_1 = 0 \qquad (1)$$

$$L_2 \frac{d^2Q_2}{dt^2} + \frac{1}{C_2} Q_2 - \frac{1}{C_3} Q_3 = 0 \qquad (2)$$

$$L_1 \frac{d^2Q_1}{dt^2} + L_2 \frac{d^2Q_2}{dt^2} + \frac{1}{C_2} Q_2 + \frac{1}{C_1} Q_1 = 0 \qquad (3)$$

These equations can be simplified as follows:

Since $I_1 = I_2 + I_3$, and since Q_1, Q_2, and Q_3 are the charges supplied by the respective currents, I_1, I_2 and I_3, then

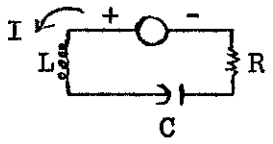
$$Q_1 = Q_2 + Q_3 \qquad \text{and} \qquad Q_3 = Q_1 - Q_2 .$$

In equations (1) and (2) above, the term Q_3 can therefore be eliminated:

$$L_1 \frac{d^2Q_1}{dt^2} + \frac{1}{C_3}(Q_1 - Q_2) + \frac{1}{C_1} Q_1 = 0 \qquad (1)$$

$$L_2 \frac{d^2Q_2}{dt^2} + \frac{1}{C_2} Q_2 - \frac{1}{C_3}(Q_1 - Q_2) = 0 \qquad (2)$$

10. A circuit where the generator output is a function of time:



Here the generator has an alternating voltage given by A sin Bt.

The equation is: $L \frac{d^2Q}{dt^2} + R \frac{dQ}{dt} + \frac{1}{C} Q = A \sin Bt.$

The student at this point should be able to analyse any circuit by these methods.

CHAPTER 16

ANALYSIS OF RESTING BEHAVIOR OF MUSCLE; MECHANICAL MODELS, PART I

A. Introductory Qualitative Statement

An understanding of the physical properties of muscle gives considerable insight into its molecular structure. Muscle can be considered as a high polymer, and to have the attributes of an instantaneous elastic response, a plastic flow, and a delayed elastic response, when subjected to a stress. These attributes can be represented by mechanical arrangements of springs, dashpots, etc., and specific models can be constructed to represent specific types of behavior of the polymer under stress. This section deals with the mathematical analysis of such models.

An instantaneous elastic response of a polymer to a tensile stress can be interpreted as being due to the deformation of the individual molecules, such as stretching primary valence bonds, opening of valence angles, or the separation of molecular neighbors against intermolecular forces.

A flow response can be interpreted as the "diffusion" of whole polymer molecules to positions of new equilibrium under stress. This is true flow which is not recoverable when the stress is removed.

A retarded elastic response can be interpreted as a change in molecular shape, such as the uncurling of molecular chains, or orientation

of the polymer molecules in relation to the stress field. This response, like the instantaneous elastic response, and unlike flow, is completely reversable. It is also referred to as the configurational elastic response.

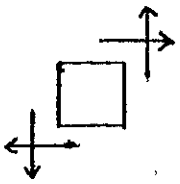
A polymer therefore may have an instantaneous stress modulus, a retarded elastic stress modulus, and a viscosity constant governing the rate of flow caused by the stress. Furthermore, a first approximation of the configurational elastic response considers it as an exponential relaxation into an equilibrium deformation. The time necessary for such relaxation is called the retardation time.

B. General Principles Concerning Mechanical Models

An object subjected to a force is said to be stressed; a stress is a force acting on the object. If the object changes shape or size as a result of the stress, it is said to be strained. There are tensile and shearing components of a stress. Those forced components acting normal to the surface being analyzed are the tensile components:

pure tensile stress, where the object is subjected to tension or compression.

Those forced components acting tangential to the surface being analyzed are called shear components:

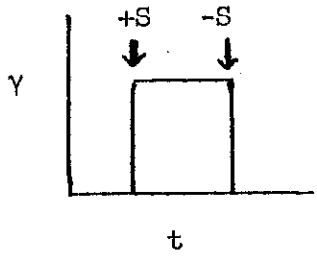


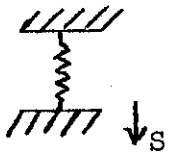
pure shear stress, where the object is subjected to shear.

In this section only the analysis of tensile stress will be considered.

a. Characteristics of an instantaneous elastic response.

If a stress force (S) is applied to an ideal elastic material, such as a spring, then the strain (γ) on the spring (or the displacement x) can be plotted as a function of time as follows:





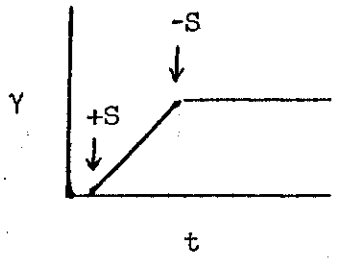
Hence:

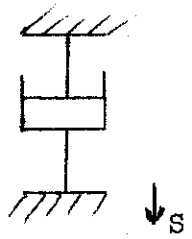
γ = elastic displacement = $\frac{1}{G}$ S where $\frac{1}{G}$ = proportionality factor, G = the tensile modulus. The rate of change of strain, or displacement is:

$$\frac{d\gamma}{dt} = \frac{1}{G}\frac{dS}{dt} \qquad \frac{dx}{dt} = \frac{1}{G}\frac{dS}{dt}$$

b. Characteristics of flow, an ideal Newtonian fluid.

If a stress (S), is applied to an ideal Newtonian fluid with viscosity η (or to a dashpot with damping R), then the strain is a function of time as:





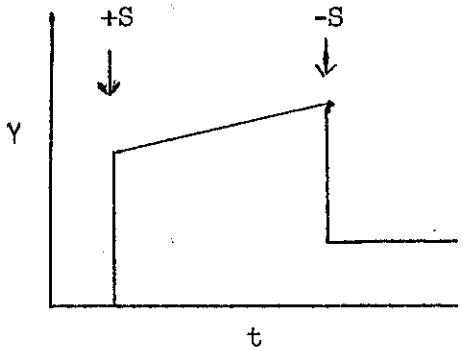
Here γ is the flow displacement, and the rate of change of strain or displacement is:

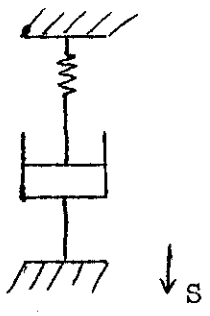
$$\frac{d\gamma}{dt} = \frac{1}{\eta} S \qquad \frac{dx}{dt} = \frac{1}{R} S$$

$$S = \eta \frac{d\gamma}{dt} \qquad S = R \frac{dx}{dt}$$

c. Characteristics of instantaneous elasticity plus flow; the Maxwell element.

If an object has the properties of instantaneous elasticity and flow under stress then:





Hence, the rate of change of the total displacement is:

$$\frac{d\gamma}{dt} = \frac{1}{\eta} S + \frac{1}{G} \frac{dS}{dt} .$$

Consider the special case where such a material above is instantaneously stressed to a certain deformation, and then constrained to retain this deformation. In this situation internal flow occurs which relaxes the stress. The change of stress with time is given as follows:

Since here $\frac{d\gamma}{dt} = 0$,

$$\frac{1}{G} \frac{dS}{dt} + \frac{1}{\eta} S = 0.$$

Solving this equation for S:

$$\frac{dS}{dt} = - \frac{G}{\eta} S$$

$$\frac{dS}{S} = - \frac{G}{\eta} dt.$$

Integrating:

$$\ln S = - \frac{G}{\eta} t + C.$$

Evaluating C: at $t = 0$, $S = S_o$, and

$$C = \ln S_o .$$

Hence:

$$\ln S = - \frac{G}{\eta} t + \ln S_o$$

$$\ln \left(\frac{S}{S_o} \right) = - \frac{G}{\eta} t$$

$$S = S_o e^{- \frac{G}{\eta} t} .$$

Therefore, it is seen that the stress relaxes exponentially with time. At time = $\frac{\eta}{G}$, then

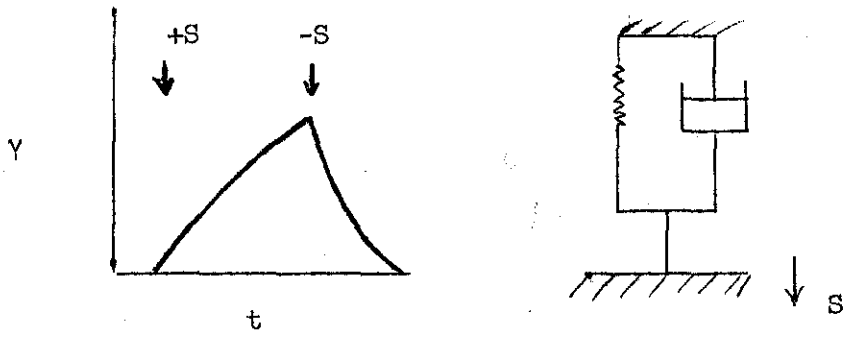
$$S = S_0 e^{-1}, \text{ or}$$

the stress will have decayed to $\frac{1}{e}$ of its original value. By definition, the ratio of $\frac{\eta}{G}$ is called the relaxation time for a material, and is symbolized by τ, so that

$$S = S_0 e^{-\frac{t}{\tau}}.$$

d. Characteristics of an object showing a retarded elastic response; the Voight element.

If a stress is applied to a material showing a retarded elastic response, the following strain-time pattern is obtained:



Since the displacement for a single spring is $\gamma = \frac{1}{G} S$, and $S = G\gamma$ (see (a) above), and since for a simple dashpot $\frac{d\gamma}{dt} = \frac{1}{\eta} S$ and $S = \eta \frac{d\gamma}{dt}$, the total stress for a Voight element is:

$$S = \eta \frac{d\gamma}{dt} + G\gamma.$$

Solving this equation for γ:

$$\frac{d\gamma}{dt} + \frac{G}{\eta} \gamma = \frac{S}{\eta}.$$

Let $\gamma = UZ$, then $\frac{d\gamma}{dt} = U\frac{dZ}{dt} + Z\frac{dU}{dt}$

$$U\frac{dZ}{dt} + Z\frac{dU}{dt} + \frac{G}{\eta}UZ = \frac{S}{\eta}$$

$$U\frac{dZ}{dt} + Z\left(\frac{dU}{dt} + \frac{G}{\eta}U\right) = \frac{S}{\eta}.$$

Setting $\frac{dU}{dt} + \frac{G}{\eta}U = 0$ and solving for U;

$$\frac{dU}{dt} = -\frac{G}{\eta}U$$

$$\frac{dU}{U} = -\frac{G}{\eta}dt$$

$$\int\frac{dU}{U} = \int-\frac{G}{\eta}dt$$

$$\ln U = -\frac{G}{\eta}t + C^1$$

$$U = e^{-\frac{G}{\eta}t} \qquad [C^1 \text{ later cancels out, so omit.}]$$

$$U\frac{dZ}{dt} = \frac{S}{\eta}$$

$$\frac{dZ}{dt} = \frac{S}{\eta U} = \frac{S}{\eta}e^{\frac{G}{\eta}t}$$

$$Z = \int\frac{S}{\eta}e^{\frac{G}{\eta}t} + C$$

$$= \frac{S}{\eta}\cdot\frac{\eta}{G}e^{\frac{G}{\eta}t} + C$$

$$= \frac{S}{G}e^{\frac{G}{\eta}t} + C.$$

Since $\gamma = UZ$

$$\gamma = \left(\frac{S}{G}e^{\frac{G}{\eta}t} + C\right)e^{-\frac{G}{\eta}t}$$

$$\gamma = \frac{S}{G} + Ce^{-\frac{G}{\eta}t}$$

at $t = 0$, $\gamma = 0$, and $C = -\frac{S}{G}$.

Hence

$$\gamma = \frac{S}{G} - \frac{S}{G} e^{-\frac{G}{\eta}t}$$

$$= \frac{S}{G}\left(1 - e^{-\frac{G}{\eta}t}\right)$$

In terms of retardation time $= \frac{\eta}{G} = \tau$,

$$\gamma = \frac{S}{G}\left(1 - e^{-\frac{t}{\tau}}\right).$$

Following the removal of the stress, the original expression:

$$\eta \frac{d\gamma}{dt} + G\gamma = S \quad \text{becomes} \quad \eta \frac{d\gamma}{dt} + G\gamma = 0.$$

Hence:

$$\frac{d\gamma}{dt} = -\frac{G}{\eta}\gamma$$

$$\frac{d\gamma}{\gamma} = -\frac{G}{\eta}dt$$

$$\ln \gamma = -\frac{G}{\eta}t + C$$

at $t = 0$, $C = \ln \gamma_0$, as $\gamma = \gamma_0$ at $t = 0$.

Thus:

$$\ln \gamma - \ln \gamma_0 = -\frac{G}{\eta}t \qquad \ln\left(\frac{\gamma}{\gamma_0}\right) = -\frac{G}{\eta}t$$

$$\gamma = \gamma_0 e^{-\frac{G}{\eta} t} = \gamma_0 e^{-\frac{t}{\tau}}, \text{ or,}$$

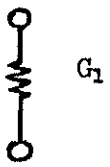
the retarded elastic element relaxes exponentially into its equilibrium shape at a rate determined by its retardation time.

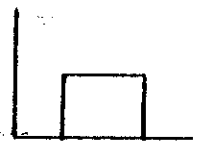
CHAPTER 17

ANALYSIS OF RESTING BEHAVIOR OF MUSCLE; MECHANICAL MODELS, PART II

A. Summary of Basic Elements

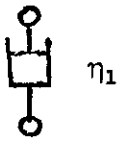
In the last chapter a number of different basic elements were presented. These are summarized at this time.

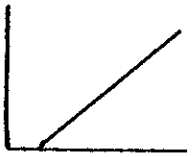
1.  G_1



$$\frac{d\gamma}{dt} = \frac{1}{G_1}\frac{dS}{dt}$$

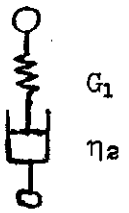
$$\gamma = S\frac{1}{G_1}$$

2.  η_1

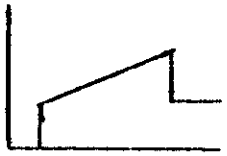


$$\frac{d\gamma}{dt} = S\frac{1}{\eta_1}$$

$$\gamma = S\frac{1}{\eta_1}t$$

3.  G_1

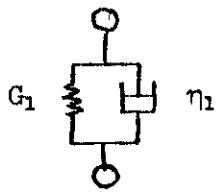
η_2

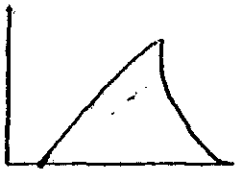


$$\frac{d\gamma}{dt} = S\frac{1}{\eta_2} + \frac{1}{G_1}\frac{dS}{dt}$$

$$\gamma = S\frac{1}{\eta_2}t + \frac{1}{G_1}S$$

4.

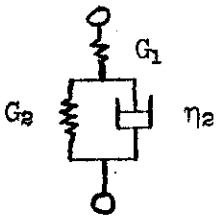




$$\frac{d\gamma}{dt} = S\frac{1}{\eta_1} - G_1\frac{1}{\eta_1}\gamma$$

$$\gamma = S\frac{1}{G_1}\left(1 - e^{-\frac{G_1}{\eta_1}t}\right)$$

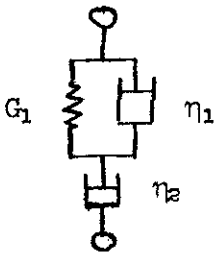
5. Instantaneous + retarded elastic response:



$$\frac{d\gamma}{dt} = \frac{1}{G_1}\frac{dS}{dt} + \left[S\frac{1}{\eta_2} - G_2\frac{1}{\eta_2}\gamma\right]$$

$$\gamma = S\frac{1}{G_1} + S\frac{1}{G_2}\left(1 - e^{-\frac{G_2}{\eta_2}t}\right)$$

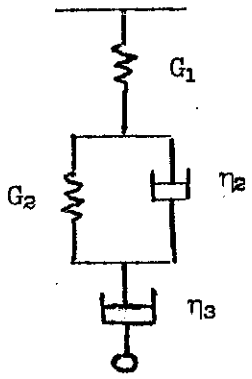
6. Retarded elastic response + flow:

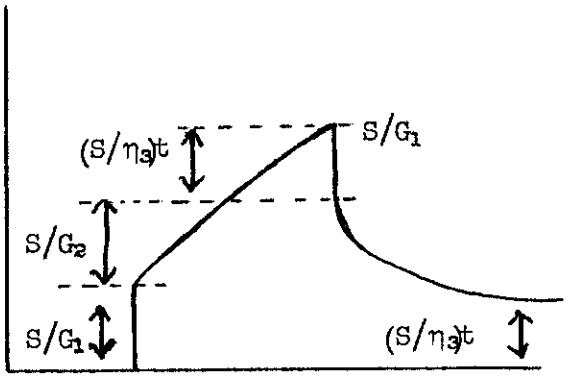


$$\frac{d\gamma}{dt} = S\frac{1}{\eta_2} + \left[S\frac{1}{\eta_1} - G_1\frac{1}{\eta_1}\gamma\right]$$

$$\gamma = S\frac{1}{\eta_2}t + S\frac{1}{G_1}\left(1 - e^{-\frac{G_1}{\eta_1}t}\right)$$

7. Instantaneous elastic response + flow + retarded elastic response:





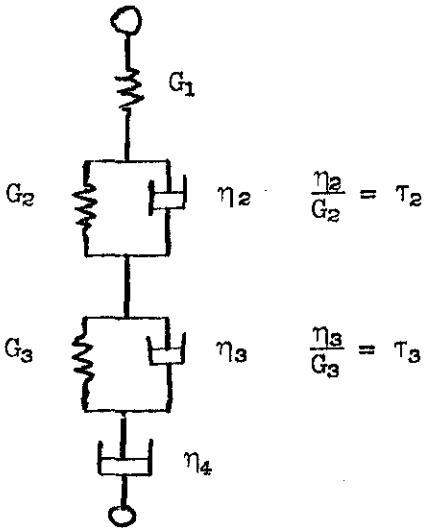
$$\frac{d\gamma}{dt} = \frac{1}{G_1}\frac{dS}{dt} + \left[S\frac{1}{\eta_2} - G_2\frac{1}{\eta_2}\gamma\right] + S\frac{1}{\eta_3}.$$

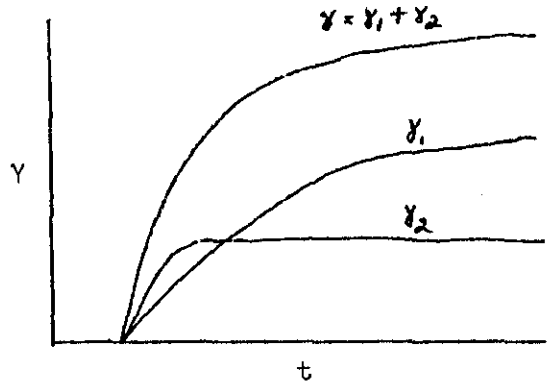
$$\gamma = S\frac{1}{G_1} + S\frac{1}{G_2}\left(1 - e^{-\frac{G_2}{\eta_2}t}\right) + S\frac{1}{\eta_3}t.$$

This is sometimes known as model A.

B. Instantaneous Elastic Response + Flow + More Than One Retarded Elastic Response; i.e., a Distribution of Retardation Times.

Consider a material exhibiting two or more different mechanisms of retarded elasticity, each with a distinct retardation time:





retarded elastic response only.

γ_1 and γ_2 are simple exponential curves, while the total response, γ, is not exponential in form.

$$\frac{d\gamma}{dt} = \frac{1}{G_1}\frac{dS}{dt} + \left[S\frac{1}{\eta_2} - G_2\frac{1}{\eta_2}\gamma\right] + \left[S\frac{1}{\eta_3} - G_3\frac{1}{\eta_3}\gamma\right] + S\frac{1}{\eta_4}.$$

$$\gamma = S\frac{1}{G_1} + S\frac{1}{G_2}\left(1 - e^{-\frac{G_2}{\eta_2}t}\right) + S\frac{1}{G_3}\left(1 - e^{-\frac{G_3}{\eta_3}t}\right) + S\frac{1}{\eta_4}t.$$

In the model above, the configurational elastic response is made up of two exponential curves of different τ. The total configurational response is described by an intermediate τ, and the response is not explicitly exponential. This is interpreted as meaning that there are two polymer molecules present of different sizes, or that there are kinks or convolutions of different sizes, as a local convolution and a long range convolution.

If the difference between τ_2 and τ_3 is not large, then the above model can be represented by model A, where

$$\frac{1}{G_{2_A}} = \frac{1}{G_2} + \frac{1}{G_3}$$

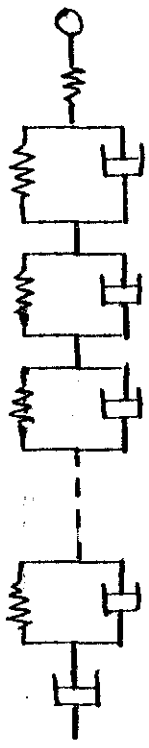
and

$$\frac{1}{G_{2_A}}\left(1 - e^{-\frac{t}{\tau}}\right) \simeq \frac{1}{G_2}\left(1 - e^{-\frac{t}{\tau_2}}\right) + \frac{1}{G_3}\left(1 - e^{-\frac{t}{\tau_3}}\right) \simeq \left(\frac{1}{G_2} + \frac{1}{G_3}\right)\left(1 - e^{-\frac{t}{\tau_{av.}}}\right).$$

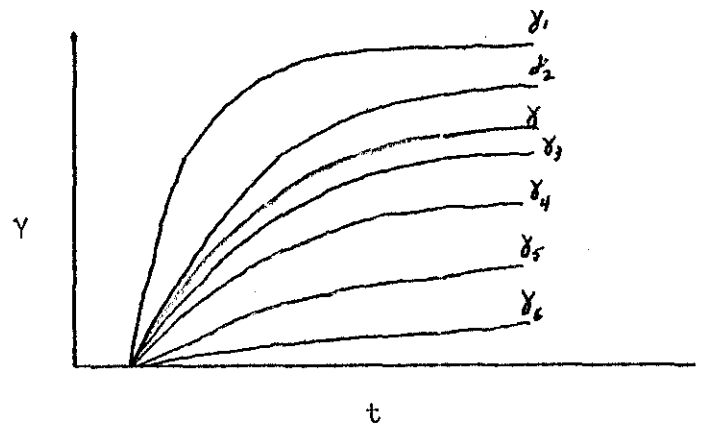
Thus the equation for the above model can be written:

$$\gamma \simeq S\frac{1}{G_1} + S\left(\frac{1}{G_2} + \frac{1}{G_3}\right)\left(1 - e^{-t\frac{G}{\eta}_{av.}}\right) + S\frac{1}{\eta_4}t.$$

In reality, a polymer would probably have a great many elements each with a specific retardation time. In other words, there may be a continuous distribution of retardation times for the configurational elasticity. The corresponding model would have a continuous set of retarded elastic elements in series. Such a model is called "model C":



Model C



Configuration elasticity for a material exhibiting a distribution of retarded elastic mechanisms.

If for model C, there are n number of retarded elastic elements, then the retardatory response is given by the sum of the n units.

$$\gamma = S \sum_{i=1}^{n} \frac{1}{G_i} \left(1 - e^{-\frac{G_i}{\eta_i} t}\right).$$

Thus the retarded deformation is the product of the stress times the sum of n retarded elastic terms, from the first term, i = 1, to the last, n.

If the above equation is expressed in terms of the reciprocal moduli, i.e., in terms of compliances, where compliance is the reciprocal of the shear or Young's modulus, $J = \frac{1}{G}$, then:

$$\gamma = S \sum_{i=1}^{n} J_i \left(1 - e^{-\frac{G_i}{\eta_i} t}\right).$$

If the number of elastic elements becomes very large, i.e., approaches ∞, and the distribution of retardation times becomes continuous, then:

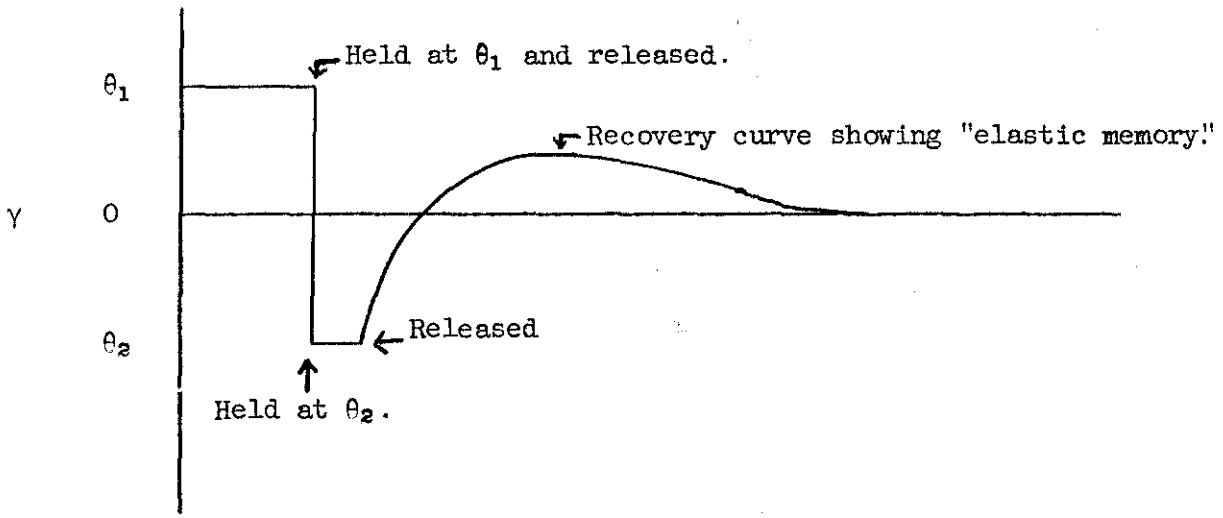
$$\lim_{\substack{n \to \infty \\ \Delta \frac{G_i}{\eta_i} \to 0}} S \sum_{i=1}^{n} \frac{1}{G_i} \left(1 - e^{-\frac{G_i}{\eta_i} t}\right) = S \int_0^{\infty} \frac{1}{G} \left(1 - e^{-\frac{G}{\eta} t}\right) d\left(\frac{G}{\eta}\right), \text{ or,}$$

$$\gamma = S \int_0^{\infty} J \left(1 - e^{-\frac{t}{\tau}}\right) d\tau,$$

in terms of compliances and retardation times. Here J is a continuous function of τ.

C. Elastic Memory

If a material possesses elements with different retardation times, then it will exhibit the phenomenon of elastic memory. Consider a material which has two delayed elastic mechanisms, one with a short retardation time and the other with a long retardation time. If such a material is stressed for a long time to a deformation θ_1, then both retarded mechanisms will reach equilibrium. If now the stress is removed, and an "opposite" stress is applied deforming the material in the opposite direction, θ_2, for a brief time, then one mechanism (with the short retardation time) will reach equilibrium, but not the other mechanism. Releasing the stress at this point will result in the material recovering beyond its true equilibrium shape, in the direction of the original stress, since the second mechanism will still be partially disposed in the direction of the original stress. In time, the material will return to its original and true equilibrium shape. The phenomenon is called "elastic memory", and can be illustrated as follows:



Most polymers exhibit the elastic memory phenomenon, and show a continuous distribution of configurational elastic responses. Since the deformation is a function of the retardation times, τ (or $\frac{\eta}{G}$), and of time t, then the equation of deformation of a material showing instantaneous elastic response, flow, and retarded elastic response, becomes a partial differential equation, i.e., the deformation γ is partially dependent upon t and partially upon τ, as follows:

Recall that the equation for a material with flow, instantaneous and retarded elastic response was:

$$\frac{d\gamma}{dt} = \frac{1}{G_1}\frac{dS}{dt} + \left[S\frac{1}{\eta_2} - G_2\frac{1}{\eta_2}\gamma\right] + S\frac{1}{\eta_3}$$

and

$$\gamma = S\frac{1}{G_1} + S\frac{1}{G_2}\left(1 - e^{-\frac{G_2}{\eta_2}t}\right) + S\frac{1}{\eta_3}t\ .$$

Now let the instantaneous elastic response be represented by γ_1, the retarded response by γ_2, and the flow response by γ_3. Hence, the deformation as a function of time is

$$\gamma(t) = \gamma_1(t) + \gamma_2(t) + \gamma_3(t).$$

Consider that $\gamma_2(t)$ represents the sum of all the individual deformations $\bar{\gamma}$, which are a function of their individual retardation times and time. Thus

$$\gamma_2(t) = \int_0^\infty \bar{\gamma}\,(\tau,t)\,d\tau$$

and

$$\gamma(t) = \gamma_1(t) + \int_o^\infty \bar{\gamma}(\tau,t)\, d\tau + \gamma_3(t).$$

Since

$$\gamma_1(t) = \frac{1}{G} S(t) \quad \text{and} \quad \gamma_3(t) = S \frac{1}{\eta_3} t(t),$$

$$\gamma(t) = \frac{1}{G} S(t) + \int_o^\infty \bar{\gamma}(\tau,t)d\tau + S \frac{1}{\eta_3} t(t).$$

The term

$$\int_o^\infty \bar{\gamma}(\tau,t)d\tau$$

is evaluated as follows:

Recall that in model A, the retarded elastic response was governed by the equation:

$$\eta \frac{d\gamma}{dt} + G\gamma = S.$$

For a continuous distribution of elastic responses, as a function of time,

S becomes S(t)

G becomes $\frac{1}{J(\tau)}$

γ becomes $\bar{\gamma}(\tau,t)$

or $G\gamma$ becomes $\frac{1}{J(\tau)} \bar{\gamma}(\tau,t)$

and $\frac{d\gamma}{dt}$ becomes $\frac{\delta\bar{\gamma}(\tau,t)}{\delta t}$

and η becomes $\frac{\tau}{J(\tau)}$

since $\eta = \frac{\eta/G}{1/G} = \frac{\tau}{1/G} = \frac{\tau}{J}$.

Hence, the retarded elastic response is now governed by the partial differential equation:

$$S(t) = \frac{1}{J(\tau)}\,\bar{\gamma}(\tau,t) + \frac{\tau}{J(\tau)}\,\frac{\delta\bar{\gamma}(\tau,t)}{\delta t}.$$

The solution of this equation yields $\bar{\gamma}(\tau, t)$, and the integral term can be evaluated.

CHAPTER 18

VISCOUS-ELASTIC PROPERTIES OF MUSCLE

A. Introduction

Having discussed the subject of mechanical models and their analysis in the last few chapters, it is now possible to turn to muscle and consider its viscous and elastic properties.

The mechanical work done when a muscle shortens against a load varies considerably with the load being lifted. It has been shown that the work done decreases rapidly as the speed of shortening increases. The work done by the muscle can be approximately expressed by the simple equation:

$$w = w_0\left(1 - \frac{k}{t}\right) \qquad (18.1)$$

where

w = work actually done

t = time taken for shortening

w_0 and k = constants.

Since a small load is lifted more rapidly than a large one, the work done decreases with decreasing loads. The relationship between load and velocity of shortening is shown in Figure 18.1.

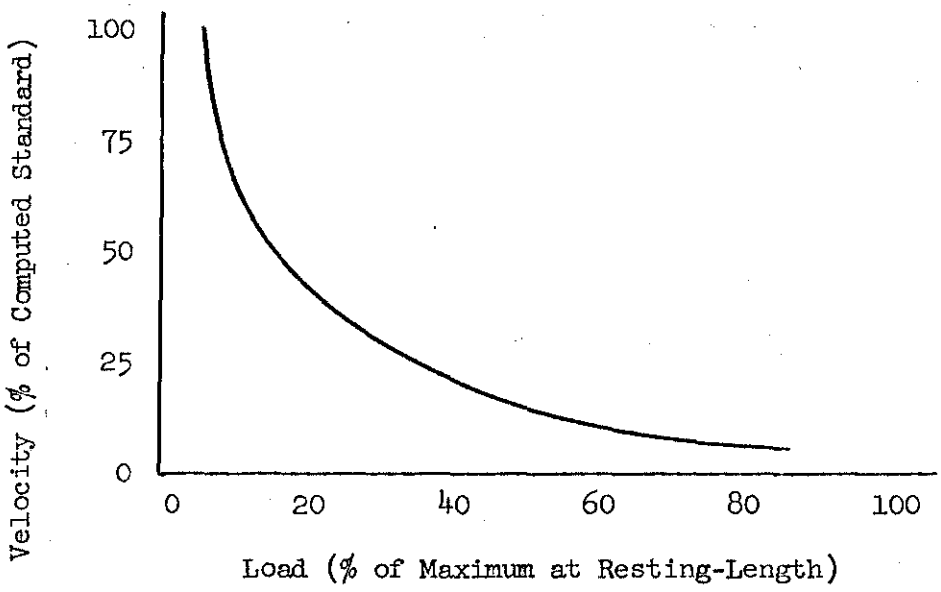
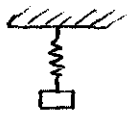


Figure 18.1 - Relationship Between Load and Velocity of Shortening.

Such a behavior in muscle is similar in many respects to the behavior of a viscous-elastic system. Equation (18.1) may be integrated in the sense that, as the result of the contractile process, the viscosity of a muscle increases so that the contraction is associated with a considerable loss of energy in overcoming internal friction. Thus, in equation (18.1), ω_o would be the ideal work to be obtained when no energy was lost by viscous resistance, i.e., the maximum work as calculated from a length-tension diagram of the muscle. Therefore, if the muscle were a simple elastic system, as a spring with a load, then the work obtainable from it would be entirely determined by the tension it developed at different lengths, and could be calculated from a length-tension diagram.



However, muscle is not a simple spring-like material, or an elastic system, but rather a viscous-elastic system. If sudden stretches are applied to a tetanized muscle, or if a tetanized muscle is allowed to contract suddenly to a shorter length, then changes in tension occur in keeping with the concept of a viscous elastic system. These changes are shown in Figure 18.2.

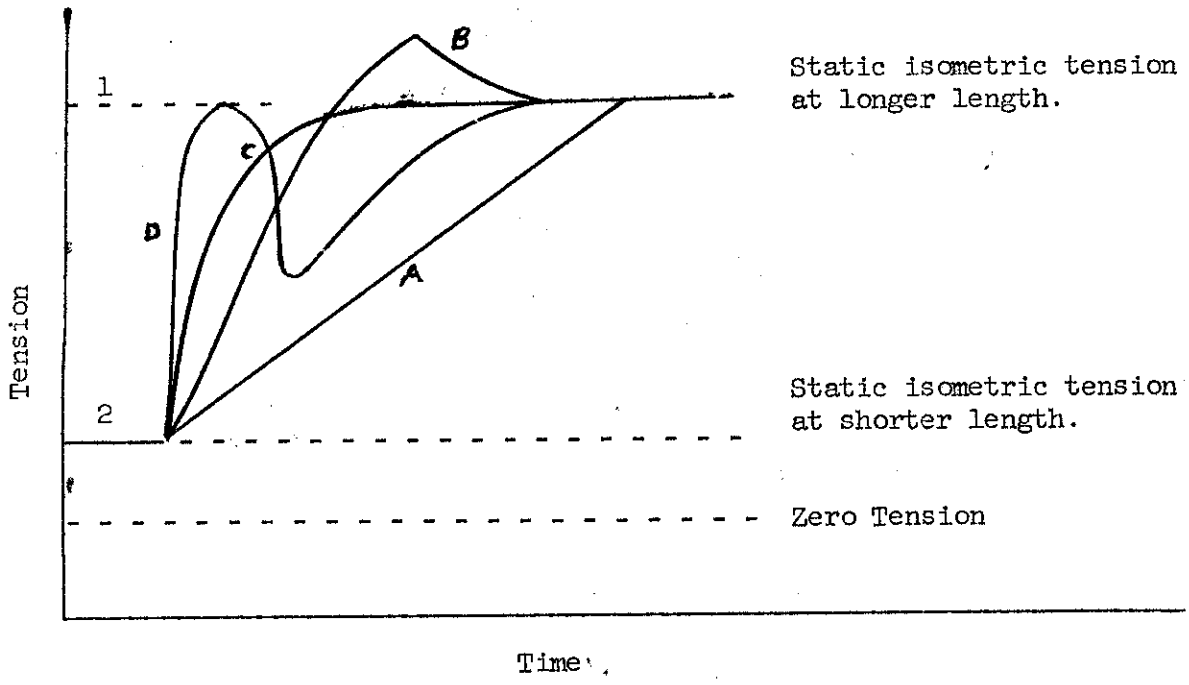


Figure 18.2 - Effects of stretching a muscle at varying speeds during a maximum tetanus.

A. Very slow stretch.

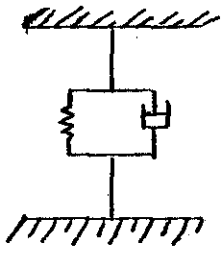
B. Fairly rapid.

D. Very rapid.

C. Intermediate between B and D.

The horizontal lines 1 and 2 of the figure indicate the static isometric tension developed by the muscle at two different lengths. Curve D shows the effect of a sudden stretch to static tension length 1, with the tension rising rapidly, but then falling rapidly to rise again slowly to a value characteristic of that length. Clearly such behavior is not that of a simple spring system. In curve B, a fairly rapid stretch is applied to the muscle, and the tension rises above the static isometric value and then approaches the latter from above. A slow stretch gives a continuous rise in tension to the new level (curve A). Curve C shows an effect intermediate between B and D. In the reverse process, a sudden release of a tetanized muscle to a shorter length causes the tension to fall almost to zero and then to rise again to a value characteristic of its new length. Only if the allowed shortening is very slow does the tension approach its new value along a straight line. In unstimulated muscle these phenomena are not observable.

Early workers attempted to explain these results by representing muscle as a simple damped spring:



B. The Levin-Wyman Model

However, it was soon pointed out that a quick release of such a system must result in a complete loss of tension, the whole at first being taken up by the viscous resistance of the dashpot. Only as the spring adopted its new length would the tension rise to the value characteristic of the new length. Recall that sudden release of a tetanized muscle results in a drop of tension, but not to zero; hence, a simple damped spring system is not an adequate concept to explain muscle behavior. Accordingly, a new model was devised, known as the Levin-Wyman model, illustrated in Figure 18.3.

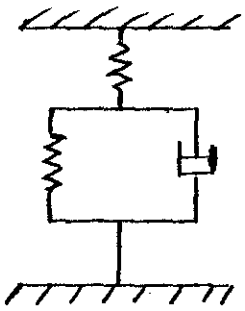


Figure 18.3 - The Levin-Wyman Model for Active Muscle.

This model consists of a damped viscous-elastic spring in series with an undamped spring. By inspection if the model is at equilibrium under a certain tension and is suddenly released, the top spring will shorten first, the lower one being unable to change its length immediately because

of the dashpot in parallel. The equilibrium between the two springs will thus be disturbed, the top spring shortening too much at first, the bottom one too little; the tension exerted at first will therefore be too small, but not zero. The new equilibrium is approached by the shortening of the lower spring and an extension of the upper one.

If the work done by the models is plotted against their speed of contraction or relaxation, then the simple damped spring system give a straight line, while the Levin-Wyman model gives an exponential curve. Results of experimental studies on muscle on the relationship between work and speed of contraction have given curves which fitted well with that predicted on the basis of the Levin-Wyman model. Thus, this model explains many features of muscle contraction, on the basis of the liberation of energy which causes the shortening of a damped spring, which, in order to develop tension outside the system, must shorten another undamped spring in series with it.

In terms of muscle structure, shortening of the myofilaments of muscle can be looked upon as the shortening of the damped spring in the model. The shortening is damped, due to the viscosity of the medium and to molecular friction. The shortening of the fibrils is associated with the stretching of connective tissue, a process similar to the stretching of a metal spring, taking place with little or no frictional loss, so that the elastic energy may be stored as potential energy during shortening.

The elastic elements of the connective tissue would thus be representative of the undamped spring of the model. The free elastic elements can be regarded as buffers, protecting the muscle against too sudden changes in tension.

The Levin-Wyman model was accepted by biologists for some time, until certain behavioral characteristics of muscle were found to be inconsistant with the model. The model envisioned contraction as a primary shortening of the damped elements which pulling against the elastic elements, stored their contractile energy as potential energy. These elastic elements were considered to do the mechanical work by subsequently shortening. On this basis then, muscle, when stimulated, would develop a given amount of heat, and would have a given amount of potential energy stored in the elastic elements. Both of these quantities would vary with the length of the fibers of the muscle. The amount of the elastic energy which could be recovered as mechanical work would bear no relation to the energy liberated. It was shown, however, that the amount of actual energy liberated by a muscle (heat plus external work) was not constant for any given initial condition of the muscle, but varied with the load, a large load resulting in the liberation of more energy than a small load. Therefore, muscle varies its output of energy according to the load, a property which is inconsistant with the Levin-Wyman model. In other words, according to the Levin-Wyman model, muscle would lift a weight by doing work on a spring

and then allowing the latter to shorten and lift the weight. But according to the experimental results, a muscle raises the weight "by a chain and windlass" mechanism; each link as it is wound up, requiring extra energy at the moment of winding. The phenomena is known as the Fenn effect.

The Levin-Wyman model subsequently encountered another difficulty, as follows. According to the model, under conditions of isotonic contraction, the rate of shortening should vary linearly with the load. In an isotonic contraction, the undamped element would be stretched until it just began to lift the weight, and after this it would retain a constant length and constant force to the end of contraction. For a particular load, the speed of contraction would be determined by the viscous elements. The same would be true for other loads, so that the speed of contraction should vary with the load in a linear fashion, following the equation:

$$P = P_o - kv \qquad (18.2)$$

where

P = load or developed tension

v = velocity of contraction

P_o = isometric tension

k = a constant

In point of fact, however, the velocity of shortening does not vary with the load in a linear manner, but rather in a non-linear fashion, as illustrated in Figure 18.1 and by the following equation:

$$P = P_o e^{-av} - kv \qquad (18.3)$$

where a is an additional constant.

Experiments show that with small loads the velocity of contraction is high, and as the load increases the velocity falls off, but not as rapidly as the Levin-Wyman model would predict. A more realistic model is one in which the energy made available for contraction increases as the load increases. Such a model can be approximated if the motion of damped spring of the Levin-Wyman model were to follow an exponential relationship between force and velocity, rather than a linear one.

CHAPTER 29

VISCOUS-ELASTIC PROPERTIES OF MUSCLE, CONTINUED

A. Activated State

During a muscle twitch, the elastic elements are stretched, and for this reason if for no other, the development of tension in muscle requires time. Clearly, the tension could be developed more rapidly if the muscle were artificially stretched during the contractile process. The actual tension which is developed, according to the modified Levin-Wyman model, depends upon the force of contraction of the damped elements. Some estimate of the force generated by these elements during a twitch can be obtained by applying stretches to the muscle at different twitch moments. The results of such a procedure are shown in Figure 19.1. The solid curves of the figure represent the isometric twitch tension at two different resting lengths. With the muscle fixed at the shorter length, stretching it to the greater length at different moments during the twitch resulted in a greater tension than that developed by stimulating the muscle at the greater length. The stretches are applied at A, B, and C, with the tension developed becoming smaller and smaller. The results simply show that the energy of the twitch is made available sooner than is indicated by the curve of isometric tension.

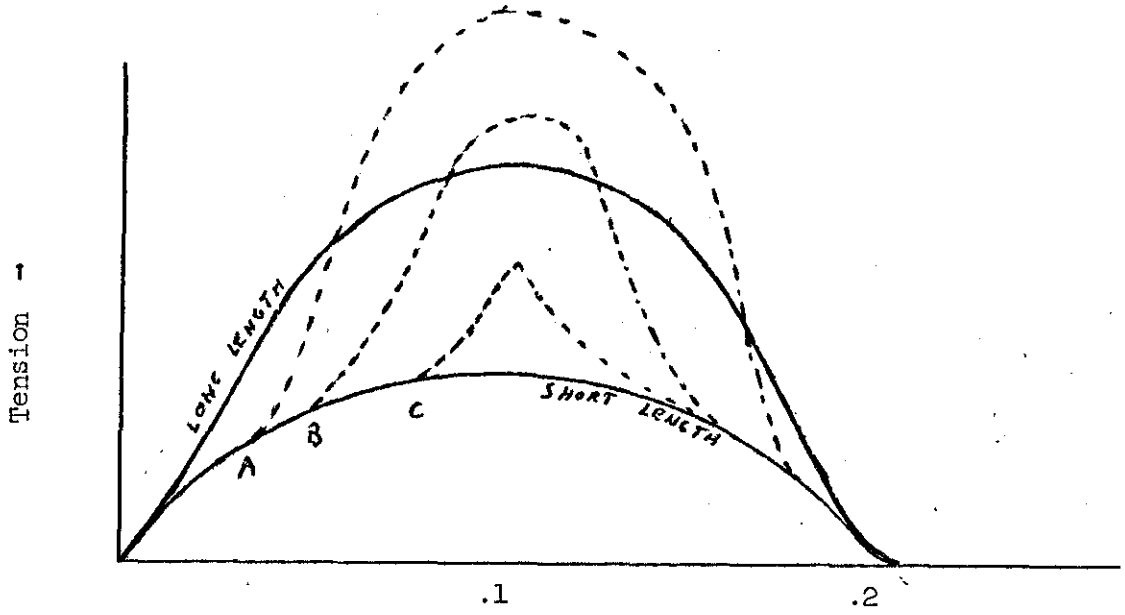


Figure 19.1 - Effect of Stretching a Muscle at Various Moments During an Isometric Twitch.

Refined experiments of this sort show that the onset of the "active state" of the contractile machinery occurs very soon after a muscle is stimulated. Thus, applying a stretch just after the end of the latent period leads to the development of a tension greater than that occuring during a tetanic contraction at the stretched length. The results are consistent with the idea that the contractile elements develop their maximal power virtually instantaneously, this maximal power being that observed in an isometric tetanus at the given length. Schematically, the relationship is shown in Figure 19.2.

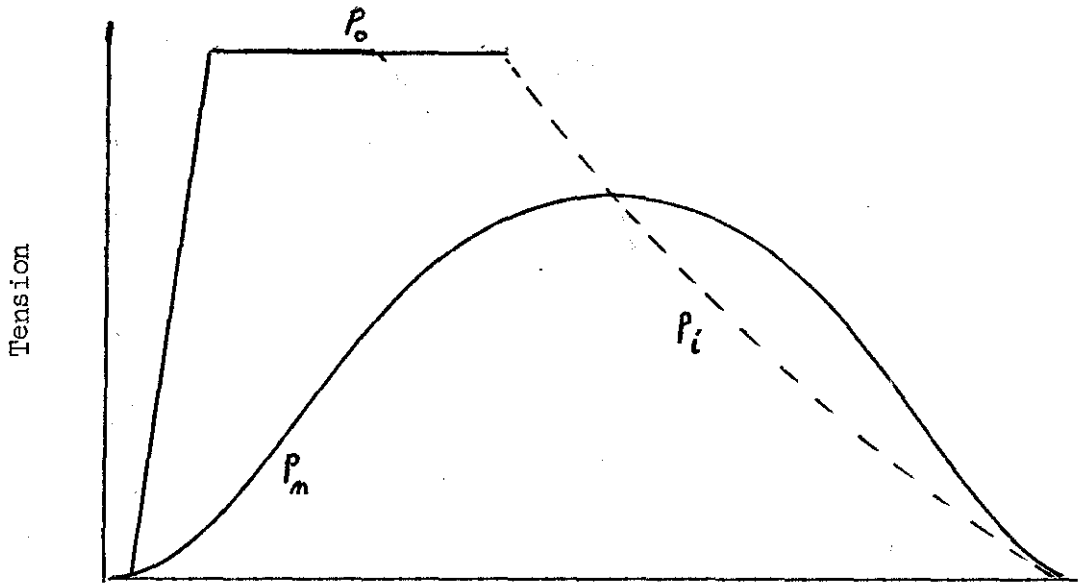


Figure 19.2 - Active State in Muscle.

In the figure, P_o represents the maximum tension that the muscle can develop, the maximal active state, established almost instantaneously, and maintained for a plateau period. After the plateau period the state declines along the dotted line indicated by P_i, which is the tension the muscle is capable of manifesting at any given moment. P_n is the tension actually recorded from the muscle. Note that mid-way in the twitch P_n becomes greater than P_i. At this point the elastic elements, which have been stretched, are now stretching the relaxing shortened contractile elements. The figure clearly indicates why tetanus-tension is greater than twitch tension.

B. Model-Muscle Structure Correlation

In the last chapter correlation of elements of a model with muscle structure was briefly considered. Such a correlation can be further developed.

The series elastic component of muscle is defined operationally as that part of the elasticity which appears to be undamped. It has been a question of whether this component resides entirely in the tendinous ends of the muscle or whether any part of it is located within the microstructure of the fibers. From experiments involving microscopic observation of the movements of different parts of a frog sartorius muscle in isometric tetanus it has been concluded that about half of the series elastic component is in the tendon and the rest in the ultimate muscle structure, possibly in the Z region of the sarcomeres. In such a preparation, hypertonic solutions eliminate stretching of the Z bands and reduce the measured series compliance to about half its normal value.

The parallel elastic component often is assumed to reside entirely in the connective tissue sheath of the muscle. In frog sartorius muscle there is a nearly exponential rise of tension with extension up to 125% of the in situ length. Beyond this point the tension rises more rapidly. Up to 125% of in situ length, the muscle warms when stretched, showing that is has properties of an imperfect rubberlike material. Beyond 125%, the muscle cools when stretched like connective tissue or any crystalline body. Since the resting tension of frog sartorius muscle at the in situ

length is small, these observations would appear to justify the representation of the parallel elastic component as a separate element of a three element model, with only a small elasticity as a property of the contractile mechanism. In this sense, then, the parallel elastic component may be treated as a separate element which has the same properties in the resting and active states and whose contribution may be subtracted in order to arrive as a measure of the tension in the contractile component. It is not to be presumed however that the same quantitative scheme holds for other types of muscles.

In terms of the sliding chain hypothesis of muscle and modern structural detail, plasticity in resting muscle can be attributed to the absence of cross-linkages between actin and myosin filaments. Also the decline of active isometric tension at lengths greater than the in situ length, or optimum length, would be related to the smaller degree of overlap and small number of cross-linkages which can form.

If the actin filaments are connected together in the center of a sarcomere by a thin elastic filament, the postulated S-filament, in the region of the H-band, then it is felt that such a filament has only weak elasticity and that it controls passive tension up to 125% of the in vivo resting length. Past this point the connective tissue elasticity would come into play. The series elastic component of active muscle would be made up of the tendon and of the A, I, and Z filaments in series, each contributing to the total, the tendon about half, the A, I, and Z components

about half. The model should also contain a friction element, ± F, which reduces the total energy available for tension, and is largely irreversable. The model is shown in Figure 19.3.

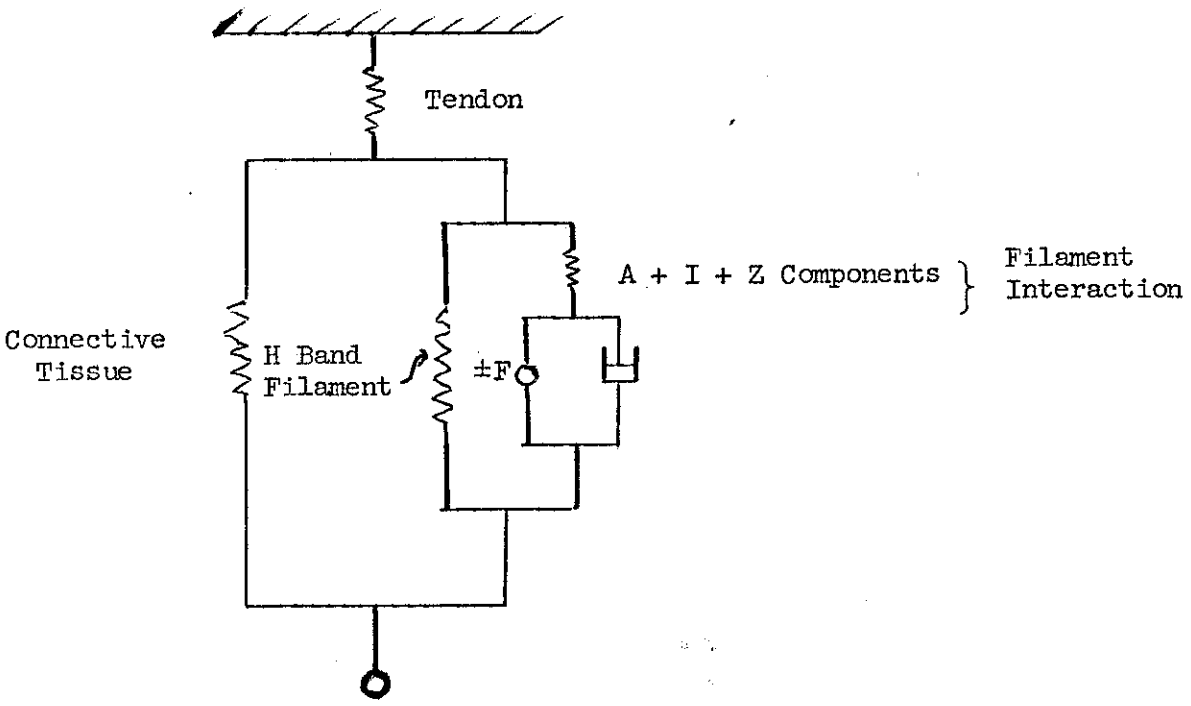


Figure 19.3 - Model of Muscle.

The mechanical properties of muscle have been represented by models consisting of springs and dashpots, arranged in series and in parallel. These models facilitate the description of muscle, but they offer no basic explanation of the events they imitate, and provide no analogy for several important properties, such as the correlation of internal viscosity with

elastic modulus, or the dependence of both on temperature. A different approach to muscle, therefore, will be considered now.

The process of stretching and relaxing a muscle can be thought of as an elastic power cycle. Basically, there are only two fundamentally different kinds of cycles possible, one involving variations of internal energy and the other variation of entropy. The two kinds of cycles are referred to as a) potential energy cycles, and b) entropy cycles or heat engines.

C. Potential Energy Cycles

A potential energy engine can be constructed with any long chain polymer in which there are mutually attractive groups disposed at intervals along the molecules, the intensity of the attractive force, and hence the elastic modulus of the material, being variable. The attraction between dipoles of the structure can be varied chemically either by affecting the magnitude of their charges or the dielectric constant of the intervening medium. When the attractive forces are strong, successive centers will approach one another and the chain will fold together and shorten. To complete the cycle the attractive forces might be decreased and the chains pulled straight again. Such a cycle can be represented by an indicator diagram as in Figure 19.4.

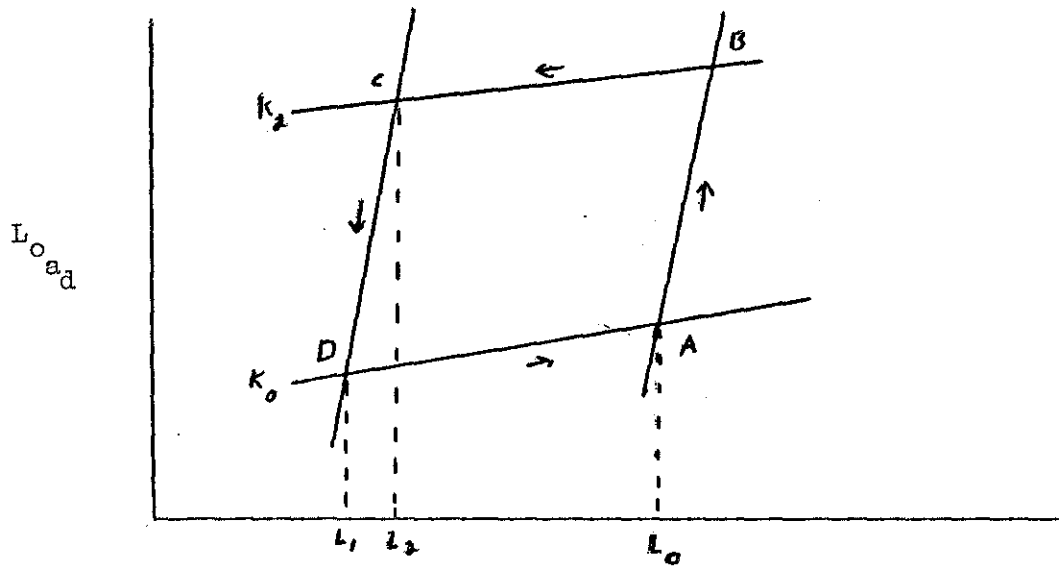


Figure 19.4 - Indicator Diagram for a Potential Energy Cycle.

If a substance begins at length L_0 under a load K_0, and if the load is increased to K_2, then the material will extend from A to B. If now the elastic modulus of the substance is increased progressively and the material allowed to shorten, then with a constant load the length will decrease to L_2, from B to C. Reducing the load to K_0, with the modulus of elasticity kept constant, the material will shorten to L_1. Reducing the elastic modulus so as to keep the load constant at K_0, extends the material to its original length L_0. The work done per cycle is represented by the area ABCD.

A mechanism of this kind for muscle has been suggested by many workers. There are, however, two serious objections to viewing muscle as performing a potential energy.

The first concerns the magnitude of the strains involved. Attractive forces between point charges fall off as the inverse square, or higher power, of the distance between their centers, and it is difficult to imagine how such forces can act except over very small distances. Yet muscle can shorten to perhaps one third to two thirds of its resting length. To account for such large strains the existence of some new kind of long range attraction must be supposed, which is possible but unlikely, or a mechanical system to magnify the motions of the contractile substance must be provided. For example, Szent Györgyi suggests that the micelles of myosin (which shortens in his theory), are closely attached throughout their length to ribbon-shaped aggregates of (a non-contractile substance) actin. When the myosin contracts, the composite strip, actomyosin, would magnify the movement in the same way as a bimetallic strip magnifies the thermal expansion of a metal. Modern structural detail of the myofibrils, however, render this view somewhat doubtful.

The second difficulty concerns the direction in which the forces act. If an increase in attractive forces is to cause longitudinal contraction, successive centers along the same chain must approach one another without too much lateral approximation of neighboring chains. Intermolecular forces are not directional, so that to ensure this effect a very regular

structure would be required of muscle. Unfortunately, the optical properties and x-ray diffraction patterns of contracted muscle do not suggest the necessary regularity.

In the next chapter the second type of elastic power cycle, the entropy cycle, will be discussed.

30.1
~~20.1~~

CHAPTER ~~20~~ 30

VISCOUS ELASTIC PROPERTIES OF MUSCLE; CONCLUDED

A. Entropy Cycles; Heat Engines

An engine operated by thermal or kinetic energy can be constructed from any material in which tension at constant length is increased by a rise in temperature. For example, a simple heat engine can be made by suspending a weight from a strip of lightly vulcanized rubber hanging between two electric heaters. If the load and the intensity of the radiation are controlled, and if the rubber is fitted with a removable insulating jacket, the system can be taken around a reversible cycle analogous to Carnot's cycle, and in Figure 20.1.

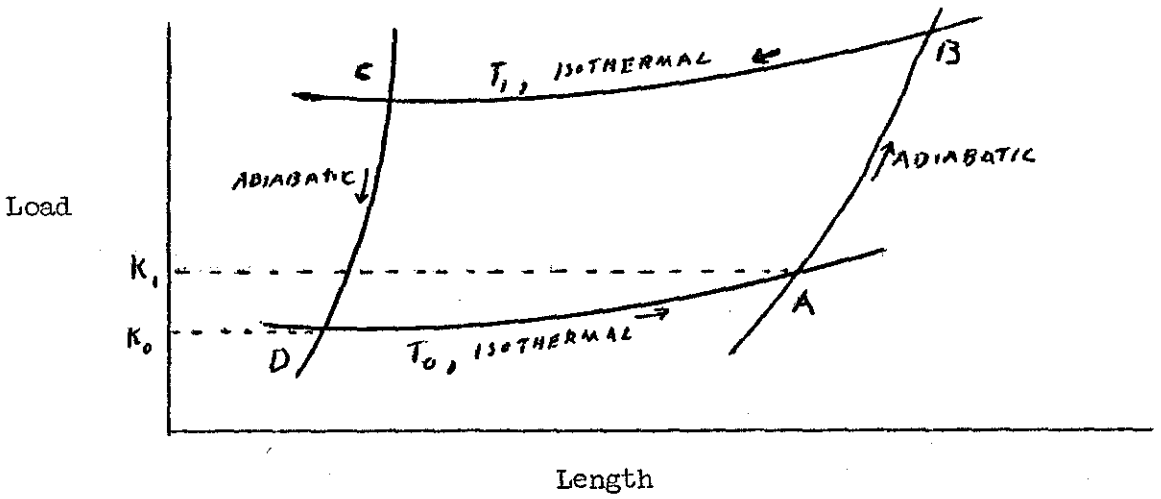


Figure 20.1 - Indicator Diagram for a Kinetic Energy or Entropy Cycle.

Starting with the rubber at a temperature T_0, under a load K_1 at A of the figure, the insulating jacket is put on and the load increased adiabatically until the temperature rises to T_1 at B. [The adiabatic process is one in which the system (rubber) is insulated from its environment; in which the system neither gains nor loses heat from its environment.] The insulating jacket is then removed and the heaters switched on; the load is decreased until the rubber has shortened to a point C, sufficient heat being supplied to keep the temperature of the rubber constant at T_1. At C the heaters are switched off, and the insulating jacket replaced, the load is decreased to K_0, and the rubber allowed to shorten adiabatically until the temperature has fallen to T_0 again. The insulating jacket is then removed, and the load gradually increased to its original value K_1, the operation being carried out so slowly that the heat produced is radiated away and the temperature remains constant at T_0.

Such a cycle can be performed on any material in which the tension/length adiabatics are steeper than the isothermals; that is, in which the thermal coefficient of tension at constant length, $\left(\frac{\partial K}{\partial T}\right)_e$, is positive. The amount of work done per cycle depends, other things being equal, on the heat capacity of the working substance. For an imperfect rubber-like material, the tension at any length may be increased as well by a decrease in the attractive forces between molecules as by a rise in temperature. The strength of intermolecular cohesion can be controlled chemically by the addition of placticizers. These become adsorbed by their polar groups onto charged

groups in the polymer, thereby concentrating the field of force of the charge within a smaller radius, and also by their bulk preventing a close approach of the chains. For strongly solvated polymers, as for example proteins swollen in water, the amount of bound solvent will also affect the mean tension in the chains, an increase in the bound solvent tending to increase the thermal energy of the chains and to decrease their cohesion. Ions which affect the swelling of a fibre may therefore be expected to affect its elastic properties as well.

By varying the concentration of plasticizer or by changing the species of ion present, a simple chemical engine can be made. Plasticizer is added or removed where heat is added or removed in the heat engine; along the adiabatics no plasticizer is allowed to enter or escape from the system, and the isothermals become plasticizer isobars along which the vapor pressure or concentration of the plasticizer is kept constant. Such a chemical engine can be constructed with any material in which the tension at constant length is increased by the addition of the plasticizer, i.e., as long as $\left(\frac{\partial K}{\partial [P]}\right)_L$ is positive.

B. Dynamic Modulus

To gain understanding about the nature of muscle, it is necessary to decide whether muscle properties resemble more of an entropy cycle or a potential cycle. This is done by subjecting muscle, or any material under investigation, to a tension of rhythmically varying intensity and recording

the resulting deformations. If the frequency is varied over a wide range, both the elastic modulus and the internal and true viscosities can be deduced.

If a material is subjected to a fluctuating load, then the amplitude of the resulting deformation will decrease with increasing frequency. The apparent modulus of elasticity as deduced from the amplitude of the response in such experiments is called the dynamic modulus. At low frequencies it approximates the modulus as measured in static experiments, and at high frequencies it increases to a maximum which approaches the range of values typical of normal solids. The relation between frequency and dynamic modulus is not linear, and the range of frequencies confined to an increase in dynamic modulus is called the critical range of frequencies.

A fall in temperature or an increase in the intensity of intermolecular cohesion will shift the critical range toward lower frequencies, since both changes tend to increase the internal viscosity. At frequencies below the critical range, where the material is behaving as a rubbery solid, either of these influences will tend to decrease the dynamic modulus, because of their effect in decreasing the static modulus. At frequencies above the critical range, when the material is behaving as a normal solid, their effect will be negligible. It becomes possible therefore to find out whether intermolecular forces have increased or decreased by comparing the relation between frequency and dynamic modulus at two stages in a cycle. Consider Figure 20.2, for example:

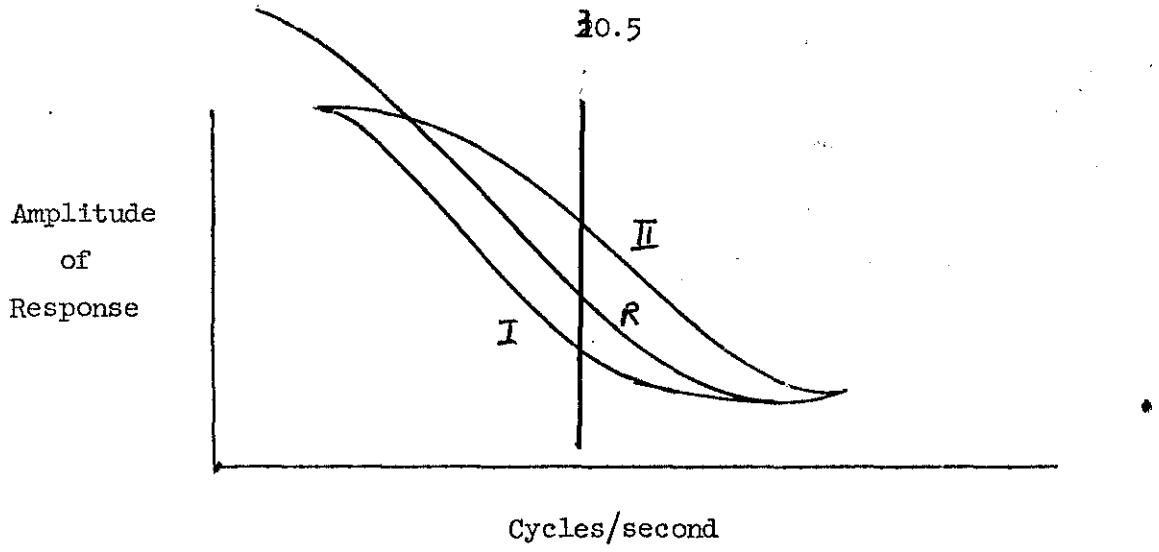


Figure 20.2 - Variations of Dynamic Modulus with Frequency.

Suppose that Curve R of Figure 20.2 applies to muscle before it contracts; if contraction is due to an increase in intermolecular forces, the critical frequency should be reduced as in Curve I, but if it is due to a decrease, the critical frequency should be increased as in Curve II. At frequencies within the critical range, as at A in the figure, the dynamic modulus should be increased on contraction in a potential cycle and decreased in a kinetic cycle. In experiments with tendons, the dynamic modulus decreases as the tendon shortens, showing that contraction is due to a decrease rather than an increase in the strength of intermolecular forces. Experiments on hair show the same results. In muscle, the dynamic modulus of both the resting and active state at any frequency decreases with increasing tension. Also, the dynamic modulus of active muscle is slightly greater than that of resting muscle at all frequencies. Sample curves are shown in Figure 20.3. The results are interpreted as follows:

In its simplest form, the potential hypothesis would lead to expect an increase in dynamic modulus at all frequencies when a muscle contracts; it can only be adapted to explain a decrease by making the hypothesis more complex. For example, a decrease in dynamic modulus on stimulation could be explained if all the load were taken by a relatively inextensible sarcolemma or by connective tissue in the resting muscle, and only was borne by the contractile mechanism when the muscle shortened. This suggestion however is questionable.

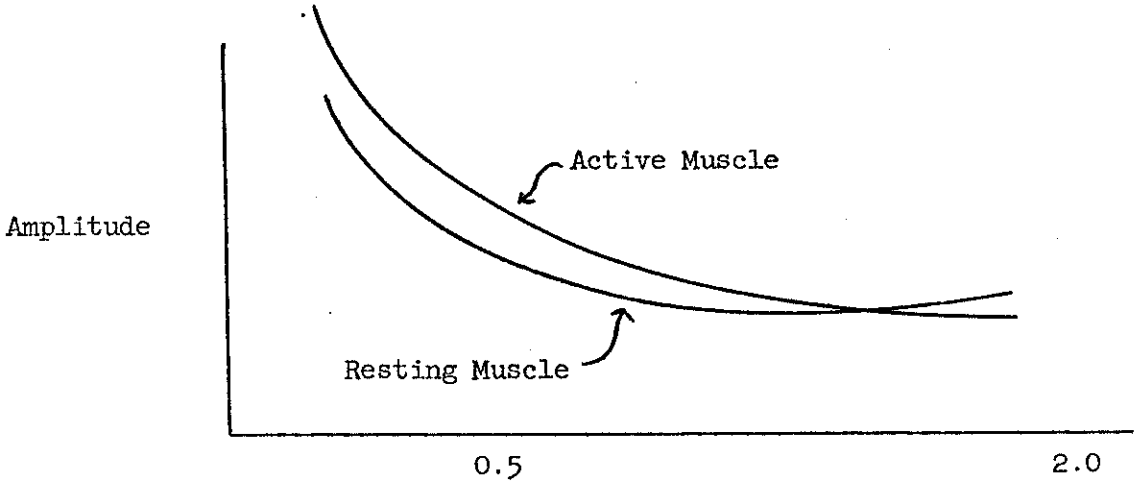


Figure 20.3 - Variations of Dynamic Modulus of Muscle.

The kinetic hypothesis seems to offer a simpler explanation. A decrease in viscosity on stimulation, and the variation of dynamic modulus with frequency are both as expected. The reversible increase in dynamic modulus with increasing tension in both active and resting muscle is typical of rubbery materials. The only detail not immediately accounted for is the

increase in dynamic modulus at frequencies above the critical range (note tail end of curves of Figure 20.3). The change is small compared with the decrease observable within the critical range, and probably reflects changes in the muscle proteins. At frequencies above the critical range the rotation and uncurling of chains is largely suppressed, and extension is due to stretching of the chains themselves, so that changes in the dynamic modulus must be a consequence of changes in the stiffness of the chains rather than of differences in the forces between them. If plasticizer molecules become attached to several consecutive polar groups along the protein molecules, it seems reasonable to suppose that they may reinforce the chains and make them less extensible.

C. Kinetic Hypothesis for Contraction

According to the kinetic hypothesis, then, the sequence of events with stimulation of a muscle would be as follows. At rest the proteins are in a partially crystalline condition, aligned parallel to the long axis of the muscle. Even in the non-crystalline parts, intermolecular attractions are strong, so that no tension is exerted, and the dynamic modulus is high. Stimulation of the muscle causes the liberation of a plasticizer, presumably ATP, which is strongly adsorbed on to the proteins and reduces the attractive forces between chains; as the strength of intermolecular attractions decreases, the tension increases. The dynamic modulus at frequencies near the critical range of resting muscle decreases as the critical range shifts

toward higher frequencies. Almost immediately after being adsorbed on to the proteins ATP is decomposed by the proteins themselves into products which are no longer capable of remaining adsorbed or of acting as plasticizers. When a muscle is in a state of sustained activity, ATP is continuously resynthesized so that the concentration of adsorbed ATP is maintained. When the stimulus ceases, the ATP present is bound in some manner.

The immediate source of energy for contraction according to this cycle is an increase in the entropy of the protein chains. In a complete cycle the ultimate source of energy is a decrease in the chemical (potential) energy of the ATP.

Most muscles posses some power of regaining their resting length, without any applied load, although the extent to which this occurs is very slight. If this power is due to crystallization, it must involve seed crystals in the form of crystalline micelles or active surfaces which have survived the process of contraction. If not opposed by any load, contraction may go so far that all the seed crystals are melted, and relaxation becomes impossible unless the muscle is stretched. Such, perhaps, is an explanation for the delta state of muscle.

D. Latency Relaxation and Plasticizer Concentration

The phenomena of latency relaxation in muscle is also explained by the entrophy cycle. (The fall in tension amounts to about 1/1,000th of the full isometric tension.) Experiments with tendon show a similar relaxation effect, apparently due to the effect of a low concentration of plasticizer in lowering the internal viscosity. A tendon or a muscle loaded with a small weight during rest will elongate very slowly. As the concentration of plasticizer increases, the rate of elongation will increase, until the concentration reaches a point at which the equilibrium load is greater than the applied load, when contraction begins. In muscle, the concentration of plasticizer rises very rapidly so that relaxation is short lived.

CHAPTER § 1

STRESS RELAXATION IN MUSCLE; AN EXAMPLE OF AN ANALYSIS OF VISCOUS-ELASTIC PROPERTIES

The decay of tension in muscle after it has been stretched and held at a constant length is called stress relaxation. The purpose of this chapter is to analyze stress relaxation curves of muscle under conditions where only contractile and series elastic components are involved; conditions where the final tension is zero or near zero.

A muscle is shortened by stimulation to a point well below the length where maximum isometric tension is developed, to a length where resting tension is zero. If the muscle is now stretched slightly, tension suddenly develops but soon decays to zero, providing the new stretched length is still well below the optimum length for tension, or where normally rest tension would still be zero.

The fall of tension following stretch is at first rapid, but then slow, and the tension decay can be expressed as the sum of two exponential curves. A typical decay curve, with tension on a logarithmic scale, is shown in Figure 21.1.

An analysis of the time course of the decay into two exponential components is given in Figure 21.2. The slow component is obtained from the slope of the linear portion of the decay curve, and extrapolated back

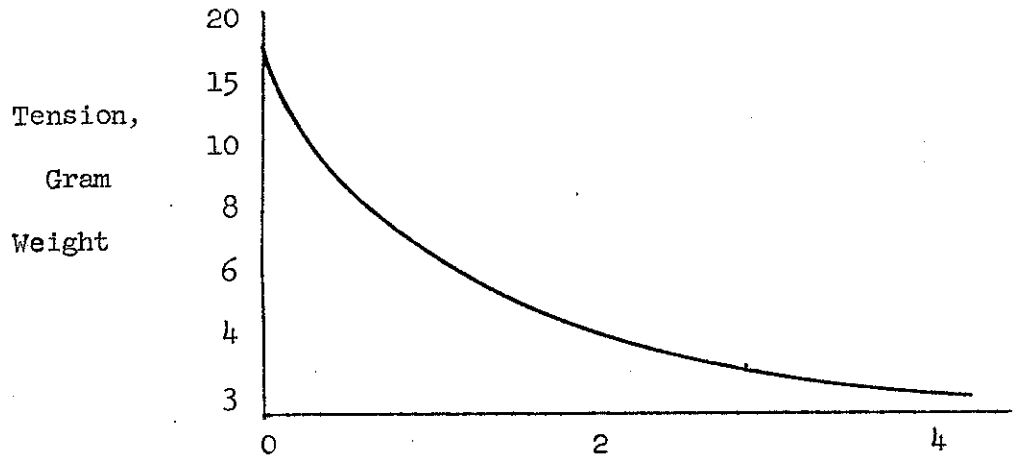


Figure 21.1 - Tension Decay Curve of Muscle Following Stretch.

to zero time. These tension values are then subtracted from those in the earlier part of the decay curve to give the time course of the fast component.

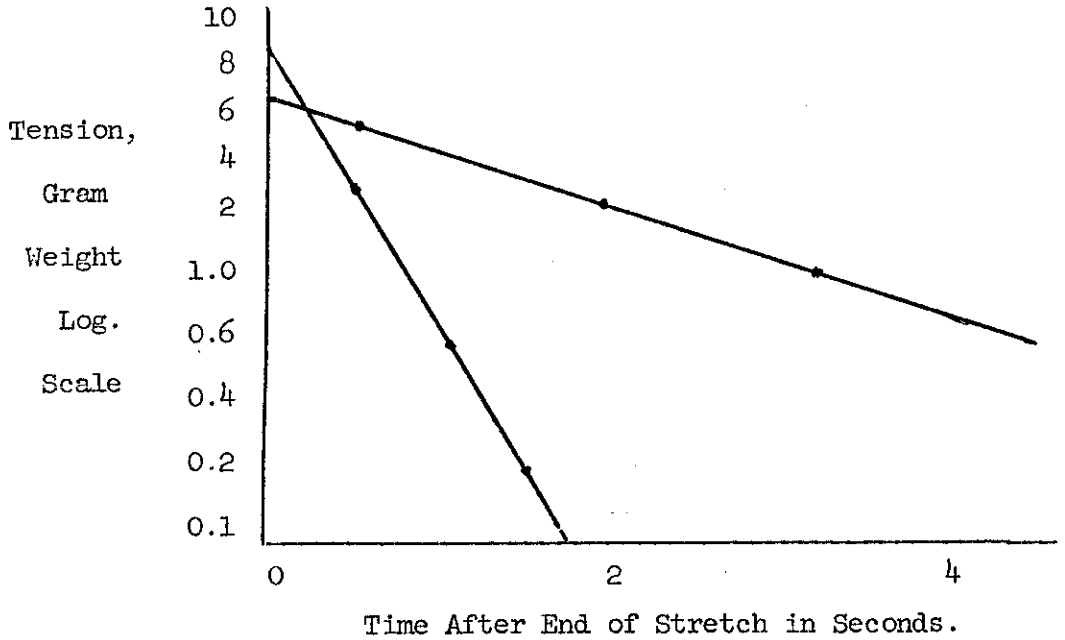


Figure 21.2 - Analysis of Tension Decay Curve into Two Exponential Components.

Since the points are on straight lines, both the fast and slow components of the total curve are exponential with time, and can be characterized by the time taken for the tension to fall to half-value.

It might be supposed that varying the speed at which the muscle is stretched would alter the time course of the decay curve. However, such is not the case, as is shown in Figure 21.3.

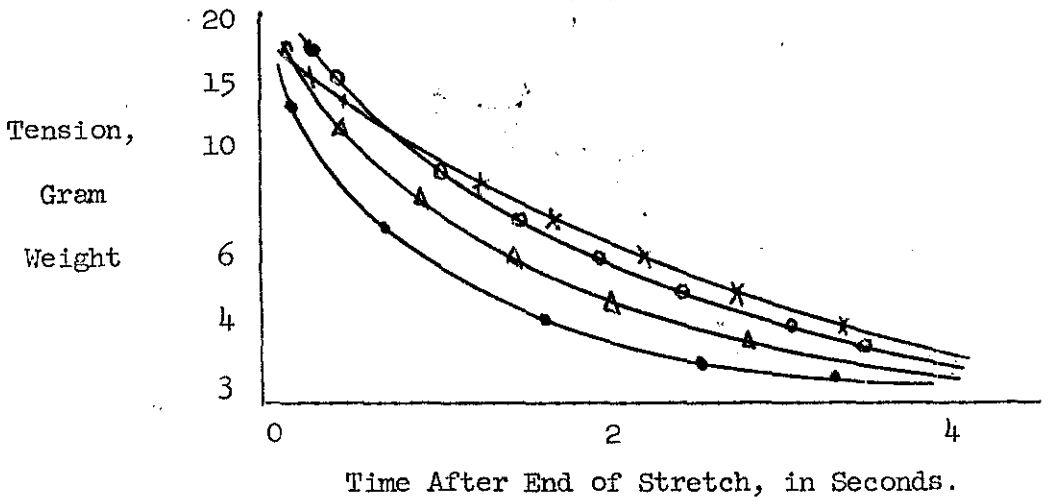


Figure 21.3 - Effect of Changing the Stretch Speed on Tension Decay Curves. O = Fast Stretch; + = Slow Stretch; • = Slower Stretch ; Δ = Slowest Stretch.

There is no obvious relation between speed of stretch and time course of tension decay. The curves of Figure 21.3 represent fifteen fold changes in speed, with only minor differences in the decay curves. In addition, changes in temperature have a negligible effect on the characteristics of the decay curve.

In any particular muscle, the half-times of the fast and slow component of the curve are very different. If such times are compared over a range of different kinds of muscle, then a relation emerges between the curves and the maximum speed at which a muscle can shorten during tetanic stimulation; i.e., the quicker the muscle can shorten the faster is its decay rate for stress-relaxation. The relation holds for both the fast and slow components of the decay curve. Figure 21.4 illustrates the relationship for a variety of muscles, using the half-times of slow components.

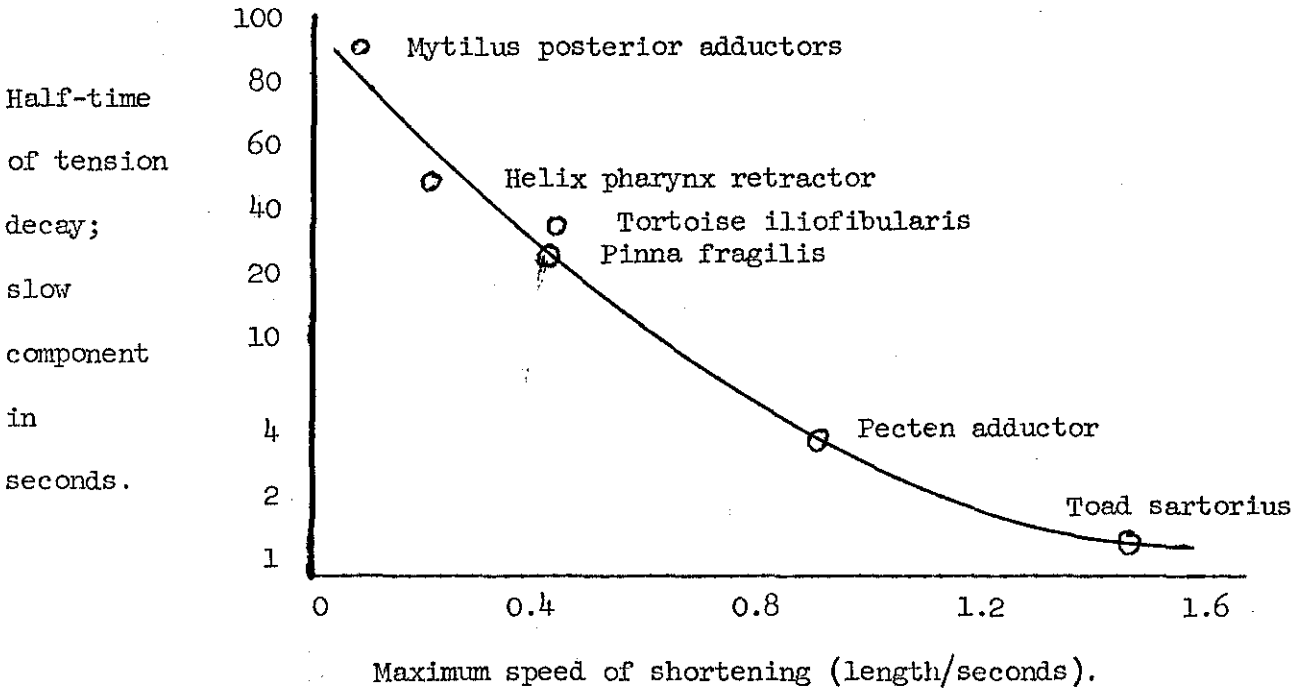


Figure 21.4 - Half-times of Slow-decay Components of Stress Relaxation Plotted Against Maximum Speeds of Shortening.

From the characteristics of the decay curves it is possible to derive a model which imitates the properties of resting muscle. For example, a stress relaxation curve containing two exponential components will be given by the stress relaxation of two Maxwell elements in parallel, as shown in Figure 21.5.

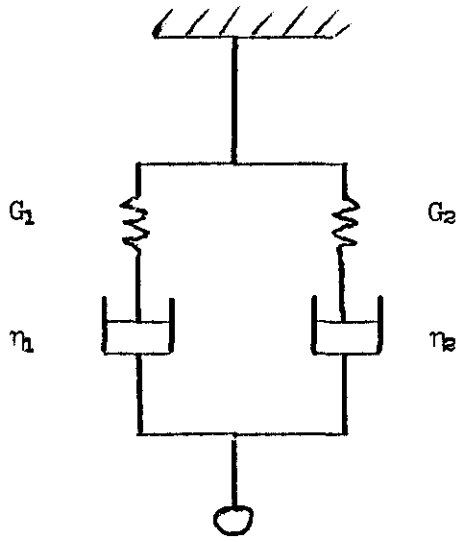


Figure 21.5 - Stress Relaxation Model

The tension or stress at any time t during the relaxation will be given by

$$S = \gamma \left(G_1 \, e^{-\frac{G_1 t}{\eta_1}} + G_2 \, e^{-\frac{G_2 t}{\eta_2}} \right).$$

Here, as before, γ = displacement, G_1 & G_2 are the spring elasticities, and η_1 & η_2 are the viscosities of the dashpots.

Note the absence in the model of parallel elastic elements. Since the decay curves were obtained at length where no resting tension is exhibited, it is justified to eliminate the known parallel elastic components from consideration. Also note that according to the model and its mathematical description, the springs obey Hooke's law, i.e., the elasticity is linear. In muscle, it is well known that the elasticity is not linear over the wide range where resting tension is produced by parallel elastic components. However, it has been shown that below length where resting tension occurs, the tension-extension relation for the series elastic component is for all practical purposes linear, and Hooke's law requirement is therefore satisfied.

The model also requires Newtonian viscosity. The fact that temperature changes have a small effect on the tension decay following stretch shows that resting muscle does not really possess simple, normal viscosity characteristics. The decay must somehow be related to molecular rearrangement within the resting contractile components as a result of flow under stress. Nevertheless, the viscous flow of muscle is closely imitated by the model.

CHAPTER 32

HEAT PRODUCTION IN MUSCLE

The relationship between the amount of work done by a muscle and the heat it produces during contraction is intimately related to the basic underlying mechanisms by which the cell chemical potential energy is transformed into mechanical work. The purpose of this and several following chapters is to examine this relationship.

The heat produced by muscle is usually separated into three main components:

1. the resting heat, which is associated with the resting metabolism of muscle;
2. the initial heat, which is produced during the actual contraction and relaxation of muscle, and
3. the recovery heat, liberated for many minutes following the cessation of activity or contraction.

A. Resting Heat

The resting heat of muscle is due primarily to the oxidation of carbohydrates. In frog sartorius muscle the heat liberated by the oxidative processes amounts to about 2×10^{-4} calories per gram of tissue per minute, and represents the rate of metabolism needed for the "static" processes of

cellular nutrition and maintenance. Such processes are linked in some unknown manner to the physical state of the muscle, since stretching a resting muscle increased by several-fold both the heat production and oxygen consumption. Some aspects of resting heat production were discussed in Chapter 5.

B. Initial Heat

The initial heat is composed of the activation and maintenance heat, (although causally both the activation and maintenance heat are identical), the shortening heat and the relaxation heat.

a. Activation and maintenance heat.

Activation and maintenance heat are correlated with the presence of the "active state", and represent the net thermal effect of the chemical processes which are responsible for muscle activity. In a twitch response, the activation heat begins sharply at the same time the mechanical state of muscle occurs, rises immediately to its maximum rate, then falls away as the active state begins to decay. In a tetanic response, the repetitive stimulation prolongs the active state and the activation heat is correspondingly prolonged.

The correlation between the active state and activation heat is not perfect, however, since the heat rate does fall off somewhat with time during a tetanic contraction, even though the active state (as measured by mechanical criteria) does not change. The activation heat also varies

with muscle length in a tetanus, but not in a twitch. From the viewpoint of muscle efficiency, the activation heat represents energy wasted, since the heat is produced whether work is done by the muscle or not. It has been said that it is the price that must be paid to hold the contractile mechanism in readiness.

b. Shortening heat

If shortening of the muscle is allowed to take place during activity, then an amount of heat is produced above the activation heat. This "excess" heat is known as shortening heat. The amount of shortening heat that is produced is proportional to the degree of shortening. The phenomena is illustrated by Figure 22.1, where in A, the muscle is activated but not allowed to shorten (isometric contraction), and in B, C, and D, increasing amounts of shortening are permitted, with increasing amounts of heat being produced.

Hence, extra heat is produced by muscle during shortening, and the amount of extra heat is directly proportional to the distance shortened.

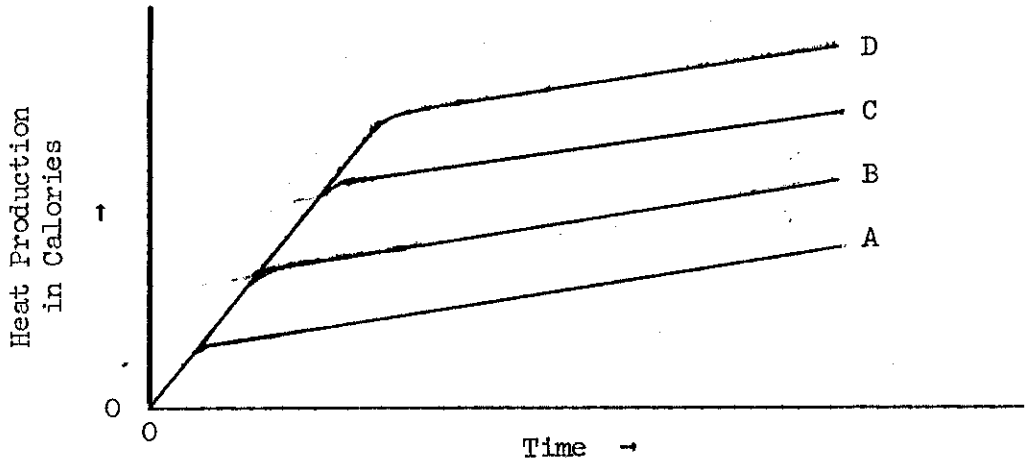


Figure 22.1 - Shortening heat production by muscle. A = isometric contraction, B, C, D, = 4, 6, and 9 mm. allowed shortening respectively.

The amount of shortening heat, although related to the degree of shortening of the muscle, is not related to the work done by the muscle. Thus, if a muscle is allowed to shorten identical distances lifting different loads, the amount of shortening heat will not vary. A constant of proportionality, $a_{thermal}$, has been defined as the amount of shortening heat per centimeter of muscle shortening. The independence of shortening heat and force on a muscle is shown in Figure 22.2.

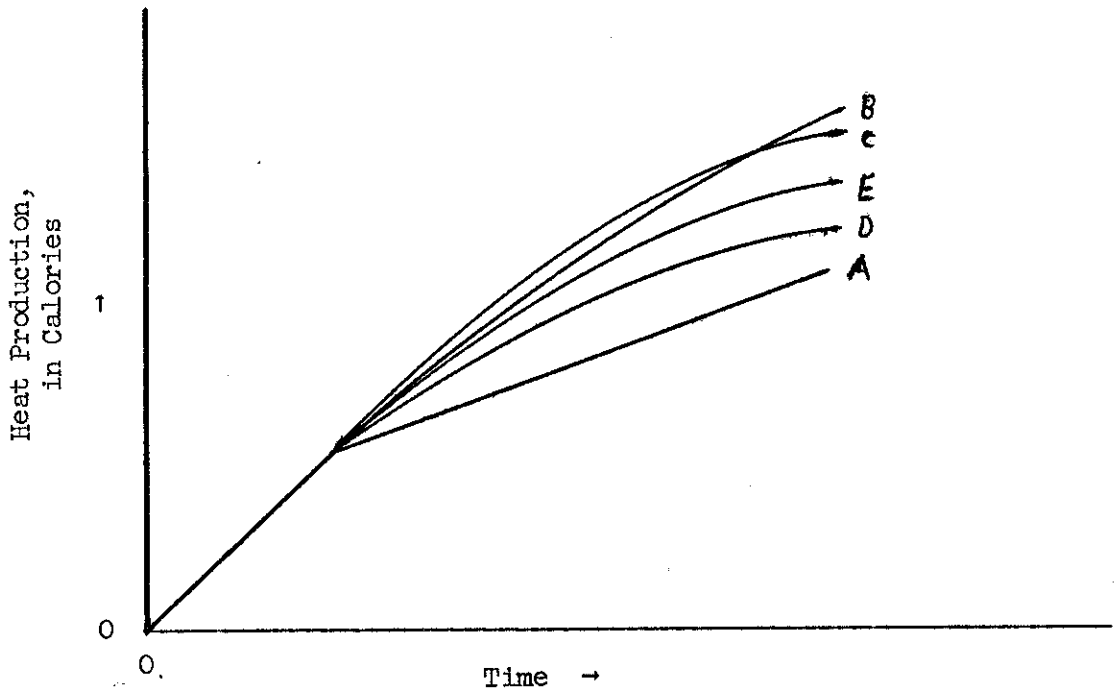


Figure 22.2 - Independence of shortening heat and muscle work. A = isometric contraction; B, C, D, and E, varying amounts of weights lifted by muscle to constant distance. The weights vary from 2 grams to 30 grams.

c. Relaxation heat

During relaxation of muscle, an additional amount of heat is liberated, and comprises the last portion of the initial heat category. This heat is not the result of active processes, but represents the degradation into heat of the mechanical energy which had been generated during contraction, and stored either in a lifted load or in a stretched elastic element. If the stored energy can be prevented from being returned to the muscle, then no relaxation heat appears.

d. Lengthening heat

Another type of heat production in muscle, which might be placed in the initial heat category, is that induced by actively stretching a muscle stimulated to contract. Contrary to expectations, perhaps, the work so done on the muscle does not appear as heat either during activity or during subsequent relaxation. Hence, work is absorped by active muscle. However, if the lengthening force on muscle is too great, then "irreversible lengthening" of the muscle is produced, and the applied mechanical work is degraded into heat. This latter effect is also seen if the force is applied to relaxing muscle, where the work on the muscle is converted quantitatively into heat. This is similar to stretching resting muscle, except that in resting muscle the amount of heat produced by stretching is actually greater than the amount of work done on the muscle.

The term "irreversible lengthening" is a misnomer, since no harm is done to the muscle in this operation. In the "reversible" range,

the heat production is actually less during isotonic lengthening (hanging a constant weight on the muscle to cause lengthening) than during isometric contraction at the same stretched length, in spite of the fact that a large amount of work is being done on the muscle by stretching. Also, the heat deficit produced is proportional to the amount of lengthening that has taken place. It has been considered that there is accordingly a negative heat of lengthening corresponding to the positive heat of shortening. Experimentation has shown however that the constant of proportionality, $a_{thermal,}$ for lengthening is some six times as great as the value for the constant for shortening. It has also been considered that work done <u>on</u> a muscle, like that done <u>by</u> a muscle, is without effect on muscle heat except indirectly through the occurrence of length changes. With these concepts, activation and shortening (or lengthening) heats would reflect independent processes in the muscle. However, experimentation does not substantiate such a simple picture. The rate of production of shortening heat can be made to vary over a wide range without effecting the activation heat, but the same cannot be done for the lengthening heat.

C. <u>Recovery Heat</u>

Like resting heat production in muscle, the last heat category, recovery heat, is due to the oxidation of carbohydrate material. Such oxidation does not occur to any great extent during the actual period of

activity, but rather follows activity at a comparatively slow rate, resynthesizing stores of organic phosphate which have been hydrolyzed during activity. As would be expected, the total amount of recovery heat produced by a muscle following activity is approximately equal to its total work production plus initial heat. For a fixed duration of stimulation more recovery heat will be produced if the muscle is allowed to shorten and do work than if it is made to contract isometrically. Beginning immediately after cessation of activity, there occurs a phasic (one minute or less in duration) absorption of heat, thought to be due to an endothermic resynthesis of ATP. The rate of oxygen consumption during the recovery period follows closely the rate of recovery heat production, and are both altered in the same manner by chemical agents or pH changes.

CHAPTER 23

HEAT PRODUCTION IN MUSCLE; HILL'S EQUATION

From the foregoing chapter, it is clear that when stimulated muscle is allowed to shorten and do work, the extra energy produced, above the isometric state, is composed of two factions, work and shortening heat. The work portion is equal to the load (P) lifted by the muscle (or force on the muscle), times the distance (x) the load is lifted; work = Px. The distance x, is, of course, equal to the distance the muscle shortens. The shortening heat, it will be recalled, is proportional to the distance the muscle shortens with the proportionality constant given as $a_{thermal}$, or simply as "a". The amount of shortening heat, then, is ax. The total extra energy produced by shortening is therefore

$$Px + ax = (P + a)x. \tag{23.1}$$

Since this expression represents the total extra energy, the derivative of the expression with respect to time represents the rate of production of the extra energy of shortening:

$$(P + a)\frac{dx}{dt} \quad \text{or} \quad (P + a)v. \tag{23.2}$$

A. V. Hill has shown that if (P + a)v is plotted against various forces on the muscle, i.e., various loads lifted by the muscle, then there is evident a linear relationship, as seen in Figure 23.1.

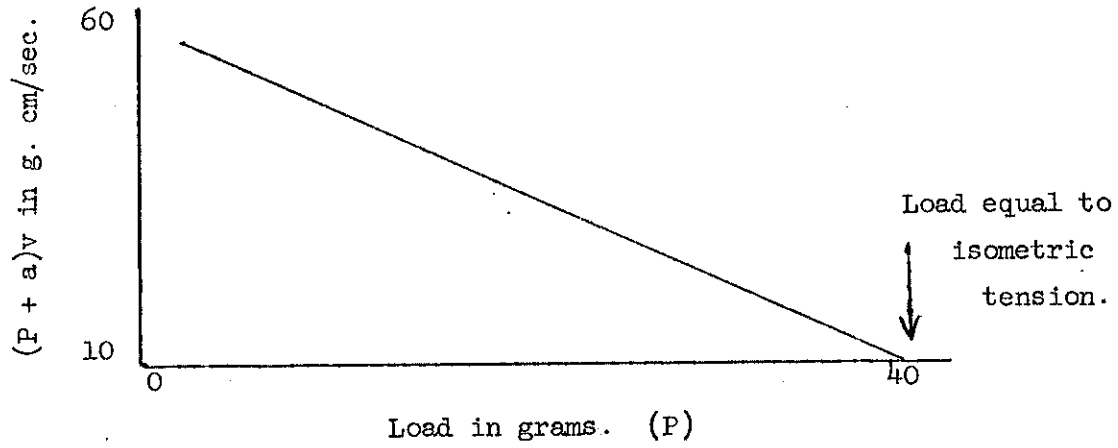


Figure 23.1 - Relationship between muscle load (P) and (P + a)v.

As shown by the figure, the greater the load, the less the rate of liberation of the extra energy of shortening. The line cuts the load or force axis at a value equal to the isometric tension. Hence the line can be characterized by the equation

$$(P + a)v = (P_o - P)b, \qquad (23.3)$$

where P_o = isometric tension, and b is a constant. Since the only variables of this equation are v and P, the velocity of shortening can be expressed as a function of the force of contraction or load. If equation (23.3) is rearranged as follows, the relationship is seen to be a rectangular hyperbola.

Write (23.3) as

$$(P + a)v = P_o b - Pb \qquad (23.4)$$

and

$$(P + a)v + Pb = P_o b. \tag{23.5}$$

Add the quantity ab to each side of (23.5):

$$(P + a)v + Pb + ab = P_o b + ab. \tag{23.6}$$

Write (23.6) as

$$(P + a)(v + b) = (P_o + a)b = \text{constant}. \tag{23.7}$$

It is easily seen that (23.7) is the equation of a rectangular hyperbola, with P and v as the variables. Experimental force-velocity curves of muscle can be fitted well by this equation, as seen in Figure 23.2.

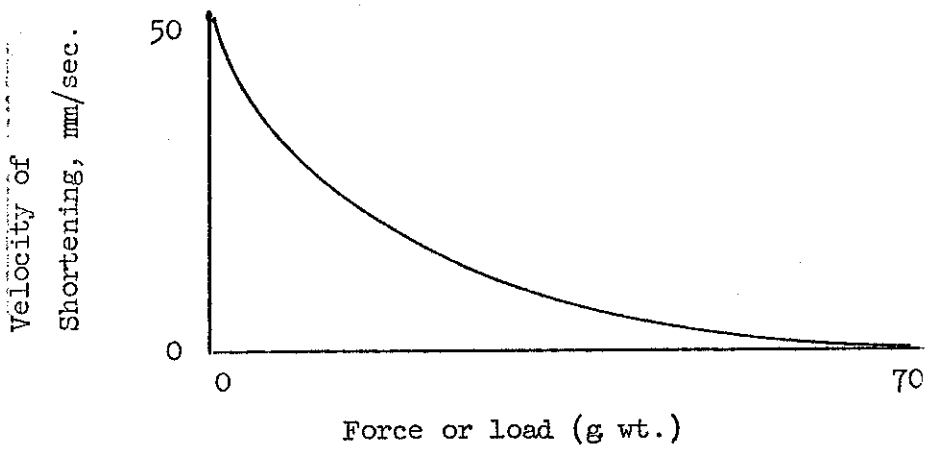


Figure 23.2 - Force-velocity Curve of Muscle.

Equations (23.3) and (23.7) are familiar forms of Hill's "classical" muscle equation. It has been shown that the same value for the constant a may be obtained either from force-velocity curves as in Figure 23.2 or from a plot of shortening heat versus distance of muscle shortening, as in Figure 23.3.

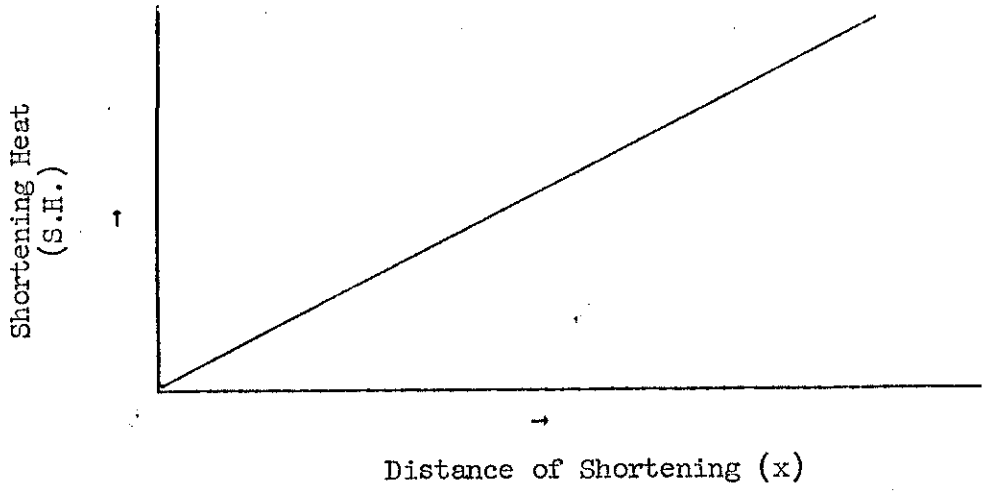


Figure 23.3 - Relation between distance of shortening and shortening heat produced, which may be used to the constant "a" from S.H. = ax.

With the use of Hill's equation, it is possible to describe the behavior of a contracting muscle under many specific mechanical conditions. For example, the time-course of tension rise in an isometric contraction can be explained as that of a contractile component (with the velocity of shortening of the component related to the load as in Hill's equation) pulling against an elastic element in series with it. At the beginning

the tension on the contractile component is small, and the component consequently shortens rapidly. As the elastic element is then stretched by the component, the tension rises, and the rate of shortening becomes less and less, with the tension rising at a progressively declining rate.

It is also possible to predict, using the equation, the behavior of muscle pulling against a Levin-Wyman lever, an inertia wheel, a combination of force and inertia, a non-linear compliance, or a combination of force, compliance and inertia. These predictions are facilitated by using an analogue circuit in which the muscle is represented by a non-linear resistance such as a rectifier, with mass as inductance, compliance as capacitance, and force as voltage.

The relationship between Hill's equation and isometric length-tension curves is as follows.

The isometric tension developed by a muscle is, of course, dependent upon the length at which the muscle is stimulated. Hill's equation is applied only to a region of the length-tension curve where the tension is maximum, i.e., where the variations of P_o with length are slight. This is a necessary requisite since P_o in the equation appears as a maximum. Also, the value of v predicted by the equation for a length-tension curve, would be the initial velocity, before shortening of the contractile components is slowed by stretching of the elastic components. However, it is possible to adjust the value of P_o so that at every instantaneous length L, P_o is given

the appropriate value $(P_o)_L$ taken from length-tension curves. If this is done, then Hill's equation can be shown to apply throughout the full extent of shortening, the equation being modified as follows:

$$(P + a)(v_1 + b) = [(P_o)_L + a]b \qquad (23.8)$$

where v_1 is the instantaneous velocity at length L. Up to the present this equation has been shown to apply only in the region of the length-tension curves below resting in vivo length.

CHAPTER 34

THEORIES OF MUSCLE CONTRACTION; INTRODUCTION

For the purpose of enhancing and perhaps maintaining interest in this book, two hypothetical schemes for contraction were outlined in Chapter 4. The remainder of the book will now be devoted to a much more detailed examination of theories for contraction. The purpose of this chapter is to present an overall picture of the general topic, and to refreshen the readers mind of some of the related material which has already been presented. Keep in mind that, although certain current theories seem impressive, a successful theory of contraction must be able to bring together the known static and dynamic structure of muscle, the magnitude and time course of mechanical events, and heat production phenomena and the chemical energetics. Such a theory has yet to be developed.

A. Mechanical Models and Viscoelastic Theory

Some of the earliest types of theories to be developed were based on viscoelastic mechanical models, many of the models mimicking the viscoelastic properties of skeletal muscle. One of the most extensive analyses of this type has been carried out by Buchthal and Kaiser. In general, isotonic contraction is described by a series of Voigt elements. Recall that a Voigt element is a spring, representing elasticity, in parallel with a dashpot, representing viscosity. Isometric contraction is described by

a series of Maxwell elements in parallel. Again recall that each Maxwell element is a spring in series with a viscosity. In such a series of parallel Maxwell elements, one of the parallel elements must be a spring without a dashpot, otherwise the model would exhibit continuous flow. Basically, an elastic element is places in series with a set of parallel elastic and viscous elements, which are in turn, placed in series with the contractile mechanism. The series elastic component includes structures such as tendon and external recording device attachments, attachments of the I band myofilaments to the Z line, and connections between I band myofilaments. Parallel elastic components include mainly the sarcolemma. Viscous elements are shared by all of these structures and by the sarcoplasm. The main objection to these mechanical models is that is is difficult to describe actual molecular mechanics in contraction, and that, as thus far developed, have not been sufficiently extensive so as to have a necessary degree of uniqueness.

B. Folding Contractile Protein Theories

Following the demonstration that actomyosin threads could be made to shorten in a test tube, theories based on the folding of the contractile proteins were constructed. The central idea of these theories was based on the known behavior of certain polyelectrolytes, which can be made to shorten and develop tension by changing their charge density. For example, at any given tension there is an equilibrium length assumed by the protein filament.

The equilibrium length is that length at which the electrostatic forces tending to repel segments of the protein and thus elongate it, are exactly opposed by entropic forces tending to fold the protein and so shorten it. Shortening of the protein occurs when the entropic (thermokinetic) forces exceed the electrostatic forces. In muscle studies, it has been found that during shortening of the contractile proteins, the entropy of the fibers increases. As was pointed out in an earlier chapter, one folding chain theory, that of Morales and associates, assumes that it is the binding of ATP by myosin that reduces the electrostatic charge density on the myosin molecule and consequently brings about shortening. The hydrolysis of ATP would take place after the contractile protein achieved the shortened form.

The folding chain theories in general are logical and intellectually satisfying, tending to explain in a rather complete way a possible mechanism for contraction and relaxation. The recent morphological evidence, however, showing that it is unlikely that myosin actually folds or shortens in contraction, has cast considerable doubt upon these theories, and they have largely been replaced by the sliding chain or "interdigitation" theories.

C. Sliding Chain Theories

It has now been rather conclusively shown by electron microscopy, that the length of the broad myofilaments in the A band (myosin) is constant and independent of stretch or contraction. (It should be mentioned that some investigators feel that the structures observed in the A band may

contain only about 60% myosin, and 40% other protein substance. Therefore it is still possible that the myosin portion does fold or shorten during contraction, with a corresponding lengthening of the other protein material present.) If it is assumed that myosin does not shorten, then it is a necessary consequence that as a fiber shortens, the myofilaments in the I band (actin) slide further into the A band between the myosin filaments. In so doing the Z lines, which are attached to the sarcolemma and I band filaments, are pulled toward the A band. That such is the case is seemingly verified by the electron microscope studies. There also appears to be little or no shortening of the I band filaments with shortening of the sarcomere up to 30%. With further shortening there occurs a buckling or folding of the I band filaments in the center of the A band; i.e., in the H band region at rest.

According to sliding model theories, the force for sliding is developed by the interposition of the actin and myosin filaments. Hence, if shortening or tension is to occur, then such interposition must be present. Recently, investigators have reported that if a muscle fiber is stretched to a length where the I filaments are pulled completely out of the A band, then electrical stimulation fails to produce shortening, in accordance with the theory.

In order to explain the nature of the force presumably generated between the filaments, theories have been developed using electrical models as analogies. For example, one such theory considers a fixed condenser

(representing one type of filament) with a movable, uncharged, rodlike mass (representing the other type of filament) positioned between the plates of the condenser. When the condenser is charged, the mass advances between the plates to a position of minimum energy. This occurs because the electric field at the ends of the condenser is curved so that the forces on the mass are not symmetrically distributed over its long axis.

A modification of this theory is as follows. Again consider two parallel plates and an uncharged rodlike mass positioned in the middle. If the plates are equally charged with the same sign and intensity, then the mass will by induction take on the opposite charge and will advance further between the plates.

Such theories, however, are quite inadequate in explaining muscle behavior. Heat evolution would be simply frictional heat, and the role of the chemical events known to take place in contraction is not evaluated.

One recent theory, that of A. F. Huxley, suggests that there might be a spacial organization of chemically active sites along the myosin and actin filaments, and that these sites might interact as they interdigitate with each other through certain critical distances. In this theory the force of contraction is proportional to the number of interactions, and the probability of interactions between pairs of sites is large when the filaments move slowly past one another and is small when they move rapidly. Hence, there would be less force with a high velocity, and the force-velocity relationship of muscle would be explained. Huxley's theory has been further developed by Weber, who has theoretically assigned definite chemical linkage

to this "sliding chemical model", by proposing that the active sites on actin are a series of SH and OH groups, forming and breaking alternately -S- and -O- bridges between myosin and actin. Podolsky, in a recent work, has added a thermodynamic basis for this model. These recent developments will now be considered in detail.

CHAPTER 35

THERMODYNAMICS OF MUSCLE; PODOLSKY'S ANALYSIS.

A. The First Law of Thermodynamics.

The first law of thermodynamics defines a relationship between the change of energy of a system transforming from state 1 to state 2, and the heat evolved from or absorbed by, and the work done by or on the system in the process of the transformation. The relationship is expressed as

$\Delta E = Q - w$ where

ΔE = the change of energy of the system, or $E_2 - E_1$.

Q = heat evolved or absorbed by the system.

w = work done by or on the system.

The pathway for the transformation from state 1 to state 2 may differ widely, and thus the quantities Q and w may differ widely, but nevertheless, the quantity $Q - w$ or ΔE will remain constant in the transformation.

For example, if a weight is attached to a stretched rubber band, and the band allowed to contract, then a quantity of work, w_1, is done. Also in the process, a quantity of heat, Q_1, would be absorbed. As an alternate path for the transformation of the rubber band from state 1, stretched, to state 2, contracted, the stretched band could be allowed to contract with no weight attached. Here $w_2 = 0$, and Q_2 would differ quantitatively from Q_1, such that $Q_1 - w_1 = Q_2 - w_2$.

As another example, consider the chemical reaction

Pyruvate + H_2 → Lactate.

In an electrochemical cell electrical work can be obtained from the reaction, ideally 11,440 calories of electrical work per mole of pyruvate. In this process, 10,200 calories of heat are evolved by the chemicals, or, −10,200 calories of heat are absorbed. Hence,

$\Delta E = -10,200 - 11,440 = -21,640$ calories.

Note that traditionally, the quantity Q is given as amount of heat absorbed, be it a + or − quantity. As an alternate pathway, the reaction or transformation could be carried out in a closed vessel with no work being obtained from the process. Here $w_2 = 0$, while the heat absorbed would be −21,640 calories. Again,

$\Delta E = -21,640 - 0$ calories.

To reiterate then, the internal energy change of a system undergoing a transformation from state 1 to state 2, is equal to the difference between the heat evolved (+ or −) and the work done (+ or −) during the transformation. Regardless of the pathway of the transformation, the quantity $Q - w$ is invariant, and depends only upon the initial and final states of the system.

This is the essence of the first law of thermodynamics. It defines the concept energy (or rather, change of energy) in terms of the quantities heat and work. It also dictates that the change of energy

around a closed path, state 1 → state 2 → state 1, must be zero. Note also, from the examples, that the internal energy of a system may be converted from one form to another, as Q to ω, yet the total amount of energy change is constant. In other words, when energy is converted from one form to another, the total energy is conserved.

Consider a chemical reaction

$$a_1 A_1 + a_2 A_2 + \cdots = \cdots + a_{s-1} A_{s-1} + a_s A_s,$$

proceeding to a <u>stage</u> of completion, or to an extent, ξ. The symbols A_1 and A_2, etc., represent reactants, or reacting substances; the symbols A_{s-1}, A_s, etc., represent the products of the reaction, the coefficients a_1, a_2, a_s, represent the stoichiometric coefficients of the reaction (i.e., the numbers needed to balance the reaction, as in $C_7H_{16} + 11O_2 \rightarrow 7CO_2 + 8H_2O$, 1, 11, 7, and 8 are the stoichiometric coefficients). From elementary chemistry, the final number of moles of either a reactant or product, N_i^1, are related to the initial number of moles of either a reactant or product, N_i, according to

$$N_i^1 = N_i + a_i \xi$$

where a_i is the change of stoichiometric coefficients, positive for products and negative for reactants.

If the change of internal energy of this chemical system, going from state 1 to a stage of completion, ξ, is designated as $\Delta E = \Delta\mu = \xi\Delta\tilde{\mu}$, where $\Delta\tilde{\mu}$ represents the change of internal energy <u>per unit extent</u> of the reaction, then the first law of thermodynamics requires that

$$\Delta\mu = \xi\,\Delta\tilde{\mu} = Q - \omega.$$

If the reaction is an isobaric process, i.e., occurs at constant pressure, P, and if the volume change accompanying the reaction is ΔV, then the work of expansion (or contraction) of the reaction is $P\Delta V$. Hence the total work, ω, can be written as

$$\omega = w + P\Delta V, \qquad \text{where}$$

w is the work done by the system in excess of the expansion work $P\Delta V$. Furthermore, the total volume change, ΔV, can be written as $\xi\, \tilde{\Delta V}$, where $\tilde{\Delta V}$ represents the volume change per unit extent of reaction. Hence,

$$\xi\, \tilde{\Delta \mu} = Q - w - \xi P \tilde{\Delta V}$$

and

$$\xi(\tilde{\Delta \mu} + P\tilde{\Delta V}) = Q - w.$$

In classical energetics, the change of energy and $P\Delta V$ terms are combined into another quantity, ΔH, called the change in enthalpy. Accordingly, the above equation can be written

$$\xi\, \tilde{\Delta H} = Q - w. \tag{25.1}$$

Here, the quantity $\tilde{\Delta H}$ represents the change of thermal energy per unit completion of the reaction when w = 0. The heat change can be positive in an exothermic reaction, or negative in an endothermic reaction. It is seen from equation (25.1), that the extent of a chemical reaction can be calculated simply by

$$\xi = \frac{1}{\tilde{\Delta H}} (Q - w) \qquad \text{where}$$

the quantity $\frac{1}{\tilde{\Delta H}}$ is a proportionality constant, assumed not to depend upon ξ.

B. Application of the First Law of Thermodynamics to Muscle.

The Work Quantity.

In the contraction of muscle, a series of chemical reactions are believed to be coupled to a mechanism capable of generating tension and producing mechanical work. Schematically this can be diagramed as follows:

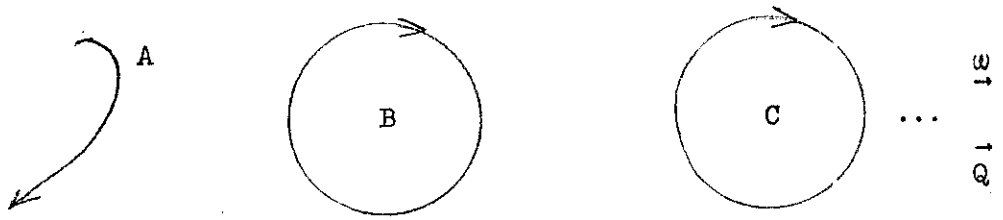


Figure 25.1 - Reaction Scheme for Initial Processes of Muscular Contraction.

Consider that A represents the net change in the extent of a chain of reactions leading to the development of tension by a muscle. B and C represent coupled processes, cyclic in nature, between the chemical reactions characterized by A, and the system generating the tension. This is to say that if a muscle is stimulated to activity, then certain chemical reactions occur to an extent ξ, and heat production and work accomplished can be measured from the muscle. Yet it is assumed that intermediate processes or reactions, B and C, have occurred, which, by the time the measurements of heat and work have been completed, have been rebalanced

to the initial state by reverse processes, -B and -C, etc. For example, the breakdown of ATP might occur to an extent ξ with stimulation of a muscle, while the cyclic making and breaking of bonds on active sites on myosin and actin might represent processes B and C.

In such a series of linked reactions, the amount of chemical energy made available for contraction is proportional to the extent of reaction A, and the rate at which the energy is made available in the active state of muscle depends on the rate of reaction A. But, since reactions A, B, and C are coupled, any reaction in the chain can be rate limiting to the development of muscle tension. Thus if reaction C were directly coupled to the contraction mechanism, and if reaction C was limited by some property of the contraction mechanism, then this property would also control the rate of reaction A, (providing the limited rate of C is less than A), since A can proceed no faster than C. Furthermore, if B and C return to their initial state by the time heat and work measurements are taken, then these cyclic reactions do not affect the overall energetics or thermodynamic equations of the system, since ΔE around a closed path is zero.

In order to measure the heat production and work performed by a muscle, recall that there exists a hyperbolic relationship between the load P on a muscle and the velocity of shortening, such that the greater the load the slower the rate of shortening. Since, in an isotonic contraction, the velocity of shortening is constant, P also represents the tension

developed by the muscle. The experimental curve is matched by Hill's empirical equation

$$(P + a)v = b(P_o - P), \qquad (25.2)$$

where a and b are muscle constants, Po is the isometric tension. For the following analysis, it is assumed that the muscle is stretched in the resting state to approximately natural body length, and that the amount of shortening which occurs with activation is small, so that heat and work properties that are a function of length can be neglected. In other words, it is assumed that the muscle length remains in the region of the broad maximum of the length-tension curve. With this assumption, the tension developed by the muscle can be expressed as a function of the velocity of shortening, by rearranging equation (25.2):

$$P = \frac{bP_o - av}{v + b} \qquad (25.3)$$

Now consider that the work, w, which the muscle does in contracting, is equal to the load, P, lifted through a distance x, or

$$w = Px.$$

Differentiating both sides of this equation with respect to time, gives the rate at which the muscle does work, or the power of the muscle:

$$\frac{dw}{dt} = P\frac{dx}{dt} = Pv. \qquad (25.4)$$

If both sides of equation (25.3) are multiplied by velocity,

$$Pv = \frac{v(bP_o - av)}{v + b}$$

then the power of the muscle can be expressed as

$$\frac{dw}{dt} = Pv = \frac{v(bP_o - av)}{v + b}, \qquad (25.5)$$

and is a function of the speed of shortening. With this expression, the thermodynamic quantity work can be evaluated in terms singly of velocity. The quantity heat will be evaluated in the next chapter.

CHAPTER 26

THERMODYNAMICS OF MUSCLE; PODOLSKY'S ANALYSIS, continued.

A. Application of the First Law of Thermodynamics to Muscle. The Heat Quantity.

As muscle shortens, energy leaves the system not only as work but also as heat. In an earlier chapter it was pointed out that the portion of heat produced by contracting muscle, above isometric heat production, is proportional to the amount of shortening, and that it does not depend upon the velocity of contraction.

The total heat production of muscle, Q, is the quantity of heat produced during isometric contraction, q_o, plus the heat of shortening, written as ax. Thus

$$Q = -(q_o + ax)$$

If this equation is differentiated with respect to time, then

$$\frac{dQ}{dt} = -\left(\frac{dq_o}{dt} + a\frac{dx}{dt}\right),$$

or

$$\dot{Q} = -(\dot{q}_o + av) \qquad (26.1)$$

As was pointed out in an earlier chapter, the constant of proportionality a, is dimensionally and numerically the same as the "a" in the force-velocity relation. Equation (26.1) shows that the rate of heat production by muscle is a function of the speed of shortening, v.

B. Characteristics of the Chemical Kinetics of Muscle

Recall equation (25.1), where

$$\xi \, \Delta\tilde{H} = Q - w \tag{25.1}$$

Let this equation be differentiated with respect to time:

$$\dot{\xi} \, \Delta\tilde{H} = \dot{Q} - \dot{w} \, . \tag{26.2}$$

Note that expressions for $\dot{Q}$ and $\dot{w}$ have been derived in equations (26.1) and (25.5). Hence (26.2) can be written:

$$\dot{\xi} \, \Delta\tilde{H} = -\dot{q}_o - av - \frac{v(bP_o - av)}{v + b}$$

or

$$-\dot{\xi} \, \Delta\tilde{H} = \frac{\dot{q}_o(v + b) + av(v + b) + v(bP_o - av)}{v + b}$$

$$= \frac{\dot{q}_o b + [\, \dot{q}_o + b(a + P_o) \,]v}{b + v} \, . \tag{26.3}$$

Equation (26.3) is an expression for the rate of reaction A, as a function of the velocity of contraction. The term $\dot{q}_o$ is a constant. The relationship between $\dot{\xi}$ and v can be seen to be hyperbolic in character if the following transformations are made.

Beginning with (26.3), multiply out the right hand term of the numerator:

$$-\dot{\xi} \, \Delta\tilde{H} = \frac{\dot{q}_o b + (\dot{q}_o v + bva + bvP_o)}{b + v} \, .$$

Replace P_o with its equivalent 4a:

$$= \frac{\dot{q}_o b + (\dot{q}_o v + bva + 4abv)}{b + v} \, .$$

Since $ab = \dot{q}_o$,

$$= \frac{\dot{q}_o b + \dot{q}_o 6v}{b + v}$$

Now, since $P_o = 4a$, to the right hand term of the numerator add $\frac{4a}{P_o}$:

$$= \frac{\dot{q}_o b + \dot{q}_o \frac{24va}{P_o}}{b + v} .$$

Dividing each term in the numerator and denominator by b,

$$= \frac{\dot{q}_o + \dot{q}_o \frac{24va}{bP_o}}{1 + \frac{v}{b}} .$$

To the right hand term of the denominator, add $\frac{4a}{P_o}$:

$$= \frac{\dot{q}_o + \dot{q}_o \frac{24va}{bP_o}}{1 + 4\frac{va}{bP_o}} . \qquad (26.4)$$

Recall that $v_{max} = v_m = \frac{bP_o}{a}$. Let the ratio of velocity to maximum velocity, $\frac{v}{v_m} = \frac{va}{bP_o}$, be called the reduced velocity. Now substitute into equation (26.4) the quantity Ψ, signifying the reduced velocity, $\frac{va}{bP_o}$:

$$-\dot{\xi}\,\Delta\tilde{H} = \frac{\dot{q}_o + \dot{q}_o 24\Psi}{1 + 4\Psi} \qquad (26.5)$$

Finally, if v is zero in (26.3), then (26.3) reduces to $\dot{\xi}_o = -\frac{\dot{q}_o}{\Delta\tilde{H}}$, and with this substitution (26.5) becomes:

$$\dot{\xi} = \dot{\xi}_o \frac{1 + 24\Psi}{1 + 4\Psi} \qquad (26.6)$$

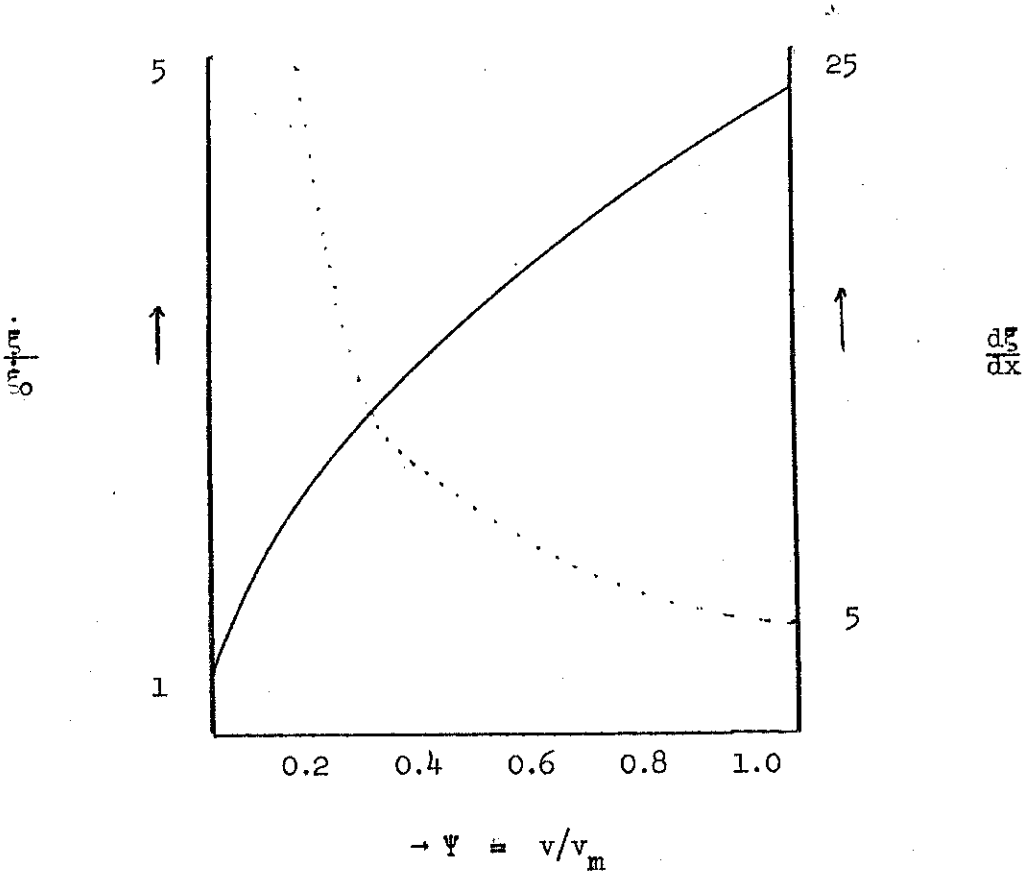


Figure 26.1 - Relative reaction rate, $\dot{\xi}/\dot{\xi}_o$, as a function of the reduced velocity of contraction, $\Psi = v/v_m$. The dotted line shows the relationship between the extent of reaction for unit distance of contraction, $d\xi/dx$, and the velocity of contraction.

Equation (26.6) clearly shows that the reaction rate for contraction is a hyperbolic function of the velocity of contraction. If this analysis is correct, then such a relationship is a requirement of any mechanochemical model, regardless of the detailed mechanism of the con-

tractile process. Figure 26.1 illustrates the relationship, with the ratio $\dot{\xi}/\dot{\xi}_o$ being plotted on the ordinate and $\Psi = v/v_m$ on the abscissa. It is seen that as the velocity increases, the relative rate of reaction, smooth curve in the figure, also increases. The dotted curve of the figure shows the relation between the extent of the driving reaction for a given distance of contraction as a function of the velocity of contraction. The function is derived from

$$\frac{d\xi}{dx} = \frac{1}{\Psi}\frac{d\xi}{dt} \tag{26.7}$$

since, with v_m a constant taken numerically as 1,

$$\frac{d\xi}{dx} = \frac{1}{v/v_m}\frac{d\xi}{dt} \qquad \text{and}$$

$$\frac{d\xi}{dx}\, v = \frac{d\xi}{dt}\,.$$

Thus $\frac{d\xi}{dx}$ is not independent of the shortening speed. If the driving reaction A was coupled directly to the displacement of the muscle, then $\frac{d\xi}{dx}$ would be independent of v. However, as $\frac{d\xi}{dx}$ increases with decreasing velocity, for a given amount of shortening, the reaction A proceeds to a greater extent, apparently, when the muscle moves slowly rather than rapidly.

One final characteristic of the reaction rate is as follows. Reconsider equation (26.3):

$$-\dot{\xi}\,\tilde{\Delta H} = \frac{\dot{q}_o b + [\dot{q}_o + b(a + P_o)]v}{v + b} \tag{26.3}$$

When v is the maximum shortening rate (taken from the force-velocity curve and $p = \frac{bP_o - av}{v + b}$ where $p \to 0$, or $v_m = \frac{bP_o}{a}$), corresponding to an unloaded contraction, the chemical reaction rate, $\dot{\xi}_m$, is calculated to increase, demonstrated by a series of transformation of (26.3):

$$-\dot{\xi}_m \tilde{\Delta H} = \frac{\dot{q}_o b + [\dot{q}_o + b(a + P_o)] \frac{bP_o}{a}}{\frac{bP_o}{a} + b},$$

$$= \frac{\dot{q}_o b + \frac{\dot{q}_o bP_o}{a} + \frac{ab^2 P_o}{a} + \frac{b^2 P_o^2}{a}}{\frac{bP_o + ab}{a}}$$

$$= \dot{q}_o b \left(\frac{a}{bP_o + ab}\right) + \frac{\dot{q}_o bP_o}{a} \left(\frac{a}{bP_o + ab}\right) +$$

$$\frac{ab^2 P_o}{a} \left(\frac{a}{bP_o + ab}\right) + \frac{b^2 P_o^2}{a} \left(\frac{a}{bP_o + ab}\right),$$

$$= \frac{\dot{q}_o a}{P_o + a} + \frac{\dot{q}_o P_o}{P_o + a} + \frac{abP_o}{P_o + a} + \frac{bP_o^2}{P_o + a}$$

$$= \frac{\dot{q}_o a + \dot{q}_o P_o + abP_o + bP_o^2}{P_o + a}.$$

Factoring the numerator,

$$= \frac{(\dot{q}_o + bP_o)(P_o + a)}{P_o + a}, \text{ or}$$

$$-\dot{\xi}_m \tilde{\Delta H} = \dot{q}_o + bP_o. \qquad (26.8)$$

Equation (26.8) can be written as

$$\dot{\xi}_m = -\frac{\dot{q}_o}{\widetilde{\Delta H}} - \frac{1}{\widetilde{\Delta H}}(bP_o), \quad \text{or}$$

$$= -\frac{\dot{q}_o}{\widetilde{\Delta H}} - \frac{\dot{q}_o}{\widetilde{\Delta H}} \frac{bP_o}{\dot{q}_o} .$$

Substituting $\dot{\xi}_o$ for $-\frac{\dot{q}_o}{\widetilde{\Delta H}}$,

$$\dot{\xi}_m = \dot{\xi}_o \left(1 + \frac{bP_o}{\dot{q}_o}\right) . \tag{26.9}$$

Hill empirically has evaluated $\dot{q}_o$ and P_o as $\dot{q}_o = ab$ and $P_o = 4a$, so that (26.9) becomes

$$\dot{\xi}_m = \dot{\xi}_o \left(1 + \frac{b4a}{ab}\right)$$

$$= 5\dot{\xi}_o \tag{26.10}$$

Thus, it is seen that the reaction rate for an unloaded contraction is five times greater than that for isometric contraction.

CHAPTER 27

THERMODYNAMICS OF MUSCLE; PODOLSKY'S ANALYSIS, CONCLUDED.

Models of the Kinematics of Contraction

The kinetics of muscle contraction described in the preceding two chapters can be incorporated into two single models in which a reaction rate depends on the relative position of two moving sites on the "contractile proteins". Recall that skeletal muscle is made up of two sets of interdigitating filaments, actin and myosin, and that when muscle shortens, the actin filaments appear to be drawn into the matrix of the myosin filaments. If the rate of one of the reactions linked stoichiometrically with the driving reaction A, Figure 25.1, depends on the position of sites on the actin filaments relative to complementary sites on the thick filaments, then the reaction rate will depend on the speed with which the actin and myosin move past each other. Thus the rate of the driving reaction is linked to the shortening speed of the muscle. Figure 27.1 pictures schematically this proposed arrangement.

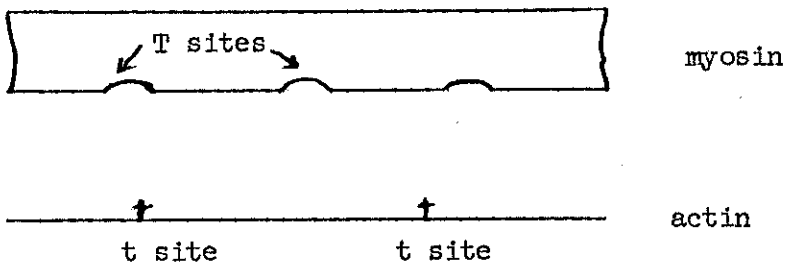


Figure 27.1 - Idealized structural model for reaction scheme.

Let the active sites on the myosin filaments be called T, and those on the actin filaments, t. Suppose that a substrate, such as ATP, is bound to the t sites, and subsequently split or hydrolized by an enzyme located on the T site, the reaction being called a T-t interaction. The probability that such an interaction could occur, k_x, would depend on the proximity of the sites to each other. Assume that as a pair of T and t sites pass each other, the interaction may or may not occur, but can occur only once. If the reaction is the rate limiting step of the series of Figure 25.1, then it controls the reaction sequence and can be equated to $\frac{d\xi}{dt}$. First, however, the kinetics of the T-t interaction must be derived, as follows:

Consider that a pair of sites move past each other with a relative but constant velocity μ, and that the distance of a t site from a T site at any time is x. If a 100% probability of interaction is equated to unity or 1, then any probability of interaction is n, and the probability that the interaction has not occurred is (1-n). For example, for a particular position x, there may be an 80% probability (.8) that the reaction has occurred, and a 20% probability (1-.8 = .2) that it has not occurred. In the next instant of time, dt, the change of probability is dn. As in a first order chemical reaction, then, the rate of change of probability is equal to a specific reaction-rate constant, k_x, time the amount of probability remaining after time t, (1-n), or

$$\frac{dn}{dt} = k_x(1-n) \qquad (27.1)$$

Since the distance (dx) of the relative positions of the sites changes in an element of time dt is dx, and since $dx = \frac{dx}{dt}\, dt = \mu dt$, equation 27.1 can be written

$$\begin{aligned} dn &= k_x(1 - n)dt \\ &= k_x(1 - n)\frac{dx}{\frac{dx}{dt}} \\ &= k_x(1 - n)\frac{dx}{\mu} . \end{aligned} \tag{27.2}$$

Therefore, the probability of interaction at any point x is given by integrating (27.2) from + to $-\infty$ of x, as follows:

Multiply out equation (27.2), as

$$\frac{dn}{dx} = \frac{k_x}{\mu} - \frac{k_x}{\mu} n \tag{27.3}$$

Rearranging (27.3),

$$\frac{dn}{dx} + \frac{k_x}{\mu} n = \frac{k_x}{\mu} \tag{27.4}$$

$$\text{Let } n = \frac{\frac{k_x}{\mu}}{\frac{k_x}{\mu}} + Z = 1 + Z. \tag{27.5}$$

$$\text{Then } \frac{dn}{dx} = \frac{dZ}{dx} . \tag{27.6}$$

Substituting for n and $\frac{dn}{dx}$ from (27.5) and (27.6) into (27.4), gives

$$\frac{dZ}{dx} + \frac{k_x}{\mu}(1 + Z) = \frac{k_x}{\mu}$$

or

$$\frac{dZ}{dx} = -\frac{k_x}{\mu} Z \ . \tag{27.7}$$

Solving for Z,

$$\frac{dZ}{Z} = -\frac{k_x}{\mu} dx$$

and

$$\int \frac{dZ}{Z} = -\int \frac{k_x}{\mu} dx$$

and

$$\ln Z + C = -\int \frac{dx}{\mu} dx \tag{27.8}$$

Evaluating C, when $\mu = \infty$, then

$$\int \frac{dx}{\mu} dx = 0$$

and

$$C = -\ln Z \tag{27.9}$$

Also when $\mu = \infty$, n (the probability for interaction) is zero so that from (27.5), Z = -1.

Hence $C = -\ln(-1)$.

Therefore (27.8) is written

$$\ln Z - \ln(-1) = -\int \frac{k_x}{\mu} dx$$

and

$$\ln\left(\frac{Z}{-1}\right) = -\int \frac{k_x}{\mu}\,dx$$

and

$$\frac{Z}{-1} = e^{-\int_{-\infty}^{\infty} \frac{k_x}{\mu}\,dx}$$

Letting $\lambda = \int_{-\infty}^{\infty} k_x\,dx$, then

$$Z = -e^{-\frac{\lambda}{\mu}}. \qquad (27.10)$$

Substituting this value of Z into (27.5),

$$n = 1 - e^{-\frac{\lambda}{\mu}}. \qquad (27.11)$$

It is clearly seen from (27.11) that as the velocity of shortening increases, the probability of reaction decreases. This is qualitatively similar to the extent of reaction per unit of shortening, $d\xi/dx$, which also decreases with increasing velocities. The term k_x has been called a specific reaction-rate constant, but its value may vary with x, so that $\int_{-\infty}^{\infty} k_x\,dx$ represents the area under the interaction probability curve, which may or may not be symmetrical about x.

To apply (27.11) to contracting muscle it is assumed that the reacting sites on each set of filaments are distributed, though perhaps

with uneven spacing, with uniform linear density, and that each T-t interaction is independent of interactions of neighboring sites or of previous transits. Two models for contraction will be considered, a sliding and a folding model. In the sliding model, the contraction force arises from interaction between actin and myosin, while in the folding model, the force arises from a change in the elasticity of the actin filament. In this model the ends of the actin filament must be fixed relative to the myosin filament. In both models, contraction is accompanied by a shortening of the I band, with the A band remaining constant.

In the application of (27.11), the sliding model will be considered first. Let the rate of shortening of the muscle, the velocity of shortening, in muscle lengths per second, be v. The velocity at which the active sites move past each other must then be half as great as v since the rate of contraction of an I band, comparable to muscle shortening, is occasioned by the halves of a sarcomere approaching each other. If the site velocity, μ, is divided by the sarcomere length, then $v = \frac{2\mu}{S}$ in muscle lengths of shortening per second. Furthermore, if the distance between t sites is L, then each T site will be presented with μ/L sites per unit of time. In other words, if μ is 10 cm./second, and the distance between t sites is .2 cm., then in one second each T site will be presented to $\frac{10}{.2} = 50$ sites. Therefore, if M is the number of t sites per cubic centimeter of muscle, and n is the probability of reaction between T and t, then $M \times \frac{\mu}{L} \times n$ = the interaction rate per centimeter of muscle.

Since the rate of chemical reaction is finite at zero velocity, $\dot{\xi}_o$, the rate is expressed as

$$\dot{\xi} - \dot{\xi}_o = \frac{M\mu}{L}\left(1 - e^{-\frac{\lambda}{\mu}}\right). \qquad (27.12)$$

In terms of speed of shortening of the ends of the muscle, substituting $Sv/2$ for μ, (27.12) becomes

$$\dot{\xi} - \dot{\xi}_o = \frac{MSv}{2L}\left(1 - e^{-\frac{2\lambda}{Sv}}\right) \qquad (27.13)$$

Considering the folding model, the ends of the actin filaments are made fixed relative to the myosin filaments. With activation, the actin filaments fold, pulling the myosin filaments closer together. It is assumed that the actin folding is linear, and that the region of folding is interdigitated with the myosin filament. At the fixed end, the relative velocity of T to t sites will be zero, and will have the value μ at the folding region closest to the I bands. As in the sliding model, the shortening velocity of the sarcomere is 2μ. Therefore, if v is the ratio of the distance of a given t site from the fixed end to the length of the folding region, its relative velocity will be μ at the free end, 0 at the fixed end, $\frac{1}{2}\mu$ in the middle, or in general $v\mu$. A T site will be presented then with $v\mu/L$ t sites per unit of time, where L again is the distance between t sites. If it is assumed that in this model, the reaction rate at zero velocity is zero, or $\dot{\xi}_o = 0$, and if per centimeter of muscle the relative velocities at each point are summed:

$\sum_{o}^{r'} v\mu$, then

$$\dot{\xi} = \frac{M\mu}{L} \int_o^{r'} r \left(1 - e^{-\frac{\lambda}{\mu v}}\right) dr \qquad (27.14)$$

is the reaction rate per cm. of muscle, assuming again that $\dot{\xi}$ is limited by the rate of T-t interaction. The indicated integration of (27.14) is carried out as follows:

$$\dot{\xi} = \frac{M\mu}{L} \int_o^{r'} r \left(1 - e^{-\frac{\lambda}{\mu v}}\right) dr \qquad (27.14)$$

$$= \frac{M\mu}{L} \left[\int_o^{r'} r\, dr - \int_o^{r'} r\, e^{-\frac{\lambda}{\mu r}} dr \right]$$

$$= \frac{M\mu}{2L} - \frac{M\mu}{L} \int_o^{r'} r\, e^{-\frac{\lambda}{\mu r}} dr. \qquad (27.15)$$

To evaluate the integral of (27.15) let

$$Z = \frac{\lambda}{\mu r}. \qquad (27.16)$$

Then

$$r = \frac{\lambda}{\mu Z} \qquad (27.17)$$

and

$$dr = -\frac{\lambda}{\mu Z^2} dZ. \qquad (27.18)$$

Substituting (27.17) and (27.18) into (27.15) gives

$$\dot{\xi} = \frac{M\mu}{2L} - \frac{M\mu}{L} \int_\infty^{\frac{\lambda}{\mu}} \frac{\lambda}{\mu Z} \left(-\frac{\lambda}{\mu Z^2}\right) e^{-Z} dZ$$

$$= \frac{M\mu}{2L} + \frac{M\lambda^2}{L\mu} \int_\infty^{\frac{\lambda}{\mu}} \frac{1}{Z^3} e^{-Z} dZ . \qquad (27.19)$$

The limits of the integral of (27.19) are obtained as follows: when $r = 1$, $Z = \frac{\lambda}{\mu}$, and when $r = 0$, $Z = \infty$.

Integrating the integral of (27.19) by parts, letting $U = e^{-Z}$, $dU = -e^{-Z}\,dZ$, $dV = \frac{1}{Z^3}$, $V = -\frac{1}{2}Z^{-2}$, gives:

$$\dot{\xi} = \frac{M\mu}{2L} + \frac{M\lambda^2}{L\mu}\left\{\left[-\frac{e^{-Z}}{2Z^2}\right]_{\infty}^{\frac{\lambda}{\mu}} - \frac{1}{2}\int_{\infty}^{\frac{\lambda}{\mu}} \frac{e^{-Z}}{Z^2}\,dZ\right\} \tag{27.20}$$

$$= \frac{M\mu}{2L} + \frac{M\lambda^2}{L\mu}\left\{-\frac{\mu^2 e^{-\frac{\lambda}{\mu}}}{2\lambda^2} - \frac{1}{2}\int_{\infty}^{\frac{\lambda}{\mu}} \frac{e^{-Z}}{Z^2}\,dZ\right\}. \tag{27.21}$$

Integrating the integral of (27.21) by parts, letting $U = e^{-Z}$, $dU = -e^{-Z}dZ$, $dV = \frac{1}{Z^2}$, and $V = -\frac{1}{Z}$, then

$$\dot{\xi} = \frac{M\mu}{2L} + \frac{M\lambda}{L\mu}\left\{\frac{-\mu^2 e^{-\frac{\lambda}{\mu}}}{2\lambda^2} - \frac{1}{2}\left(\left[\frac{-e^{-Z}}{Z}\right]_{\infty}^{\frac{\lambda}{\mu}} - \int_{\infty}^{\frac{\lambda}{\mu}} -\frac{1}{Z}\left[-e^{-Z}\right]dZ\right)\right\} \tag{27.22}$$

$$= \frac{M\mu}{2L} + \frac{M\lambda^2}{L\mu}\left[\frac{-\mu^2 e^{-\frac{\lambda}{\mu}}}{2\lambda^2} - \frac{1}{2}\left(\frac{-\mu e^{-\frac{\lambda}{\mu}}}{\lambda} + \int_{\infty}^{\frac{\lambda}{\mu}} \frac{e^{-Z}}{Z}\,dZ\right)\right], \tag{27.23}$$

$$= \frac{M\mu}{2L}\left[1 - e^{-\frac{\lambda}{\mu}} + \frac{\lambda}{\mu}\left(e^{-\frac{\lambda}{\mu}} - \frac{\lambda}{\mu}\int_{\infty}^{\frac{\lambda}{\mu}} \frac{e^{-Z}}{Z}\,dZ\right)\right]. \tag{27.24}$$

Equations (27.24) and (27.12) predict the kinetics for the folding and sliding models of contraction, and can be compared with that derived from the Hill equation for work and heat production (26.6).

In equation (27.12) for the sliding model, the quantities $\frac{M}{L}$ and λ are not known ($\mu = \frac{Sv}{2}$), but two values for each term can be selected such to fit two different relative velocities on Figure 26.1, and then other values of $\dot{\xi}$ calculated. The resulting curve closely approximates the hyperbolic curve of Figure 26.1, as seen in Figure 27.1. Equation (27.24) can be treated in a similar fashion, providing the last term, the exponential integral, is neglected. The results again closely approximate the curve of Figure 26.1, and is shown in Figure 27.1.

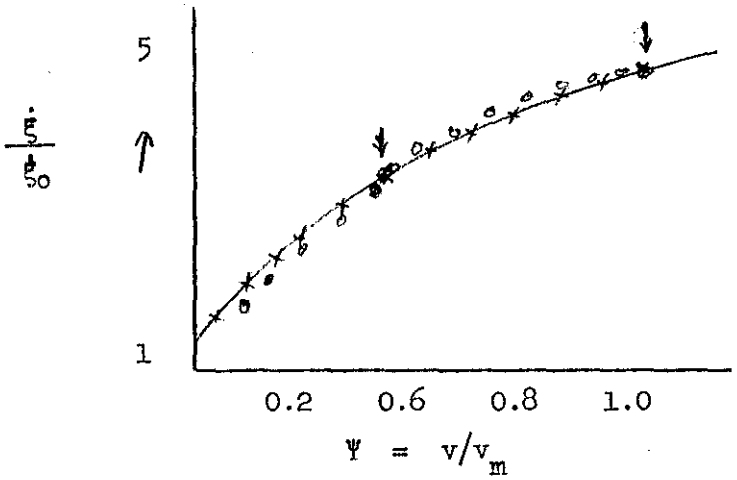


Figure 27.1 - Smooth curve: relative rate of reaction as a function of reduced velocity. Circles: predicted kinetics for sliding model. Crosses: predicted kinetics for folding model.

The close agreement shown in Figure 27.1 supports the initial hypothesis that interaction between filaments in relative motion controls the rate of the driving reaction for contraction. However, the analysis is unable to distinguish between the merits of the sliding and folding hypotheses.

Consideration of

HUXLEY'S ANALYSIS OF CONTRACTION (ref: Prog. in Biophys. 7: 255-318, 1957)

A Underlying Theory

Basic to Huxley's analysis is the concept that actin and myosin filaments interdigitate, and that the myosin filaments have attachments which slide along the main substance of the filament. The sliding or oscillating attachments are thought of as combining temporarily with sites on adjacent actin filaments, the connections forming spontaneously but broken only by an energetic reaction. The rates at which connections are made or broken are assumed to depend on the position of the sliding attachment relative to the myosin filament, and that the reactions are catalyzed by enzymes fixed to the myosin filament. Such a conceived system is illustrated in Figure 28.1 The arrows of the figure represent the relative

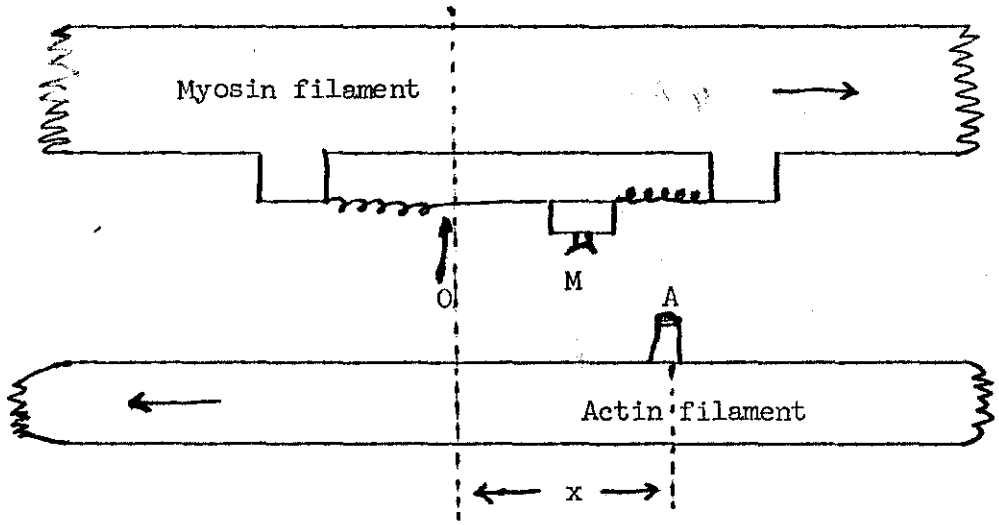


Figure 28.1 - Schematic Mechanism for Contraction.

motion of the filaments during muscle shortening. The 0 position is the equilibrium position of the M site. During shortening, the actin filament, attached to Z bands at either end, moves to the left relative to the myosin filament. The distance of A site from the equilibrium position of the M site is designated as x, and is positive if A is to the right of 0.

Let the rate constant for making a connection between A and M be f, and that for breaking the connection, g. Both of these constants, however, are to depend on x, in that as x decreases, f decreases in a linear manner (f recedes from A) to zero at 0 position, while g also decreases to zero as x decreases in a linear fashion, but is always numerically less than f.

The sequence of events would be as follows. Initially, sites M and A are detached, with M oscillating on either side of its equilibrium position due to thermal agitation. If a M-A connection is made, then tension is exerted on the actin thread, and can only happen to the right of 0. Once the M-A interaction has occurred, however, there is always a chance that it will be broken, since g is finite at all points of x, except where $x = 0$. When the A-M link passes 0 to the left, then consider that f remains zero, but g instantaneously increases to a large and constant value, so that the probability is great that the link will be broken, thus preventing tension from being exerted in the opposite direction to the shortening of the muscle.

Thus, at high rates of shortening, a large proportion of the links will not be broken in time to prevent a considerable resistance to shortening. In the sequence of events, let a high energy phosphate compound, XP,

be bound to site A, and combining with site M. After detachment of A + M, let XP be split to X and P, the fragments no longer being bound to site A. At this point it is supposed that A is to the left of the equilibrium position, and with further shortening, moves on to the next M area, while another A site moves into the original M site area. The overall A-M interactions are asynchronous. The detailed reactions are:

$$AXP + M \rightarrow AXPM \quad \text{(rate constant f)} \tag{28.1}$$

$$AXPM \rightarrow AXP + M \quad \text{(rate constant g)} \tag{28.2}$$

$$AXP \rightarrow A + X + P \tag{28.3}$$

B. Mathematical Formulation

Let there be a large number of contraction sites, all with the A site in the same relative position to O, with the same x value. Let 1 be the total number of these sites, combined or uncombined, and n the proportion combined (M with A), and (1 - n) the proportion not combined. As in first order reactions, therefore,

$$\frac{dn}{dt} = (1 - n)f - ng. \tag{28.4}$$

or the rate of change of n is the product of the rate constant f and the number of sites not combined, minus the number combined times the rate constant g for breaking the combination. Also, since $v = \frac{dx}{dt}$, where v = the

velocity at which the actin and myosin filaments slide past each other as the muscle shortens, equation (28.4) becomes:

$$-v \frac{dn}{dx} = f - (f + g)n. \tag{28.5}$$

The velocity is negative since x decreases during shortening. As in Chapter 27, in terms of the rate of shortening in muscle lengths per second, V, v is equal to sV/2, s being the sarcomere length. Thus, (28.5) can be written as

$$-\frac{SV}{2} \frac{dn}{dx} = f - (f + g)n. \tag{28.6}$$

Energetically, as a result of reactions (28.1) to (28.3), consider that one high-energy phosphate group is split off, liberating e ergs per contraction site in one cycle. Let the frequency with which A sites are presented to <u>each</u> M site be v/L, where L is the distance between A sites on the actin filament. Furthermore, since the reaction of an M site is a first order reaction, then $\frac{dn}{dt} = (1 - n)f$, where n is the probability of the reaction. Such probability, times the frequency of A sites present, or

$$n = \frac{v}{L} \int_{x = \infty}^{x = -\infty} f(1 - n)dt \tag{28.7}$$

is the number of times each M site enters a cycle of reactions per second. The limits of the integral are x = + and - ∞ since f is a function of x.

Also since →

$$\frac{dn}{dt} = -v\frac{dn}{dx} = f(1 - n),$$

and

$$dn = -\frac{1}{v}(1 - n)f\,dx,$$

equation (28.7) can be written as

$$n = \frac{1}{L}\int_{-\infty}^{\infty} f(1 - n)dx. \tag{28.8}$$

If m is the number of M sites per cubic centimeter of muscle, and e the ergs per contraction site per cycle, then the total rate of energy liberation per cubic centimer of muscle is

$$E = \frac{me}{L}\int_{-\infty}^{\infty} f(1 - n)dx \tag{28.9}$$

The tension generated by a contracting muscle is formulated as follows. Assuming that the M site attachment can be represented as a simple spring, then once an A-M interaction has occurred, the tension generated by the interaction at any point x is kx, where k is the spring stiffness coefficient in dynes/cm. The work done as the two filaments slide past each other is

$$\int_{-\infty}^{\infty} kx\,dx.$$

In a section of muscle the number of interacting sites, or probability of A-M combined sites, varies, and is a function also of x. Hence, in a section of muscle, the work generated is

$$\int_{-\infty}^{\infty} n\,kx\,dx.$$

Since work is force x distance, the force or tension generated is

$$\frac{1}{L}\int_{-\infty}^{\infty} n\,kx\,dx,$$

where L, again, is the distance between A sites. The total tension developed by a muscle is the sum of the tensions developed by all the contraction sites within one half of a sarcomere, or s/2. If the total number of M sites per cubic centimeter is m, then the number of sites responsible for the total tension is ms/2. The total tension generated per cm^2 cross-sectional area of muscle is therefore:

$$P = \frac{msk}{2L}\int_{-\infty}^{\infty} nx\,dx. \qquad (28.10)$$

In order to evaluate equations (28.6), (28.9), and (28.10), the manner in which f and g vary with x must be detailed. Figure 28.2 illustrates the basic assumption for the relationships. The figure shows that to the left of x = 0, g is a constant, g_2, while to the right of 0, g increases from 0 as x increases. f is 0 at x = 0 and to the left of x = 0, then increases at a rate greater than g to the right of x = 0. At x = h, f again drops to zero. The ordinate scale is chosen such that 1 equals the value of f + g at x = h.

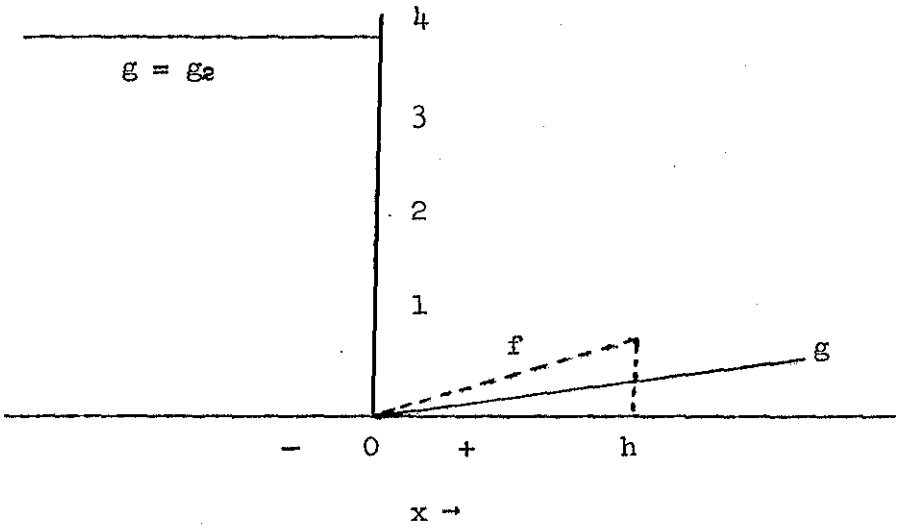


Figure 28.2 - Variations of f and g with x.

Therefore, when $x < 0$, $f = 0$ and $g = g_2$. When $x = h$, let the value of $g = g_1$. Then at $x = 2h$, $g = g_1 \frac{2h}{h} = 2g_1$; or in general when $x > h$, $g = g_1 \frac{x}{h}$ and $f = 0$.

Likewise, when $0 < x < h$, $f = f_1 \frac{x}{h}$ and $g = g_1 \frac{x}{h}$. Using these relationships, equation (28.6) can be solved.

Consideration of

HUXLEY'S ANALYSIS OF CONTRACTION, CONTINUED; SOLUTION OF EQUATIONS

Equation (28.6),

$$-\frac{SV}{2}\frac{dn}{dx} = f - (f + g)n$$

is solved for values of x, where

$x < 0$	$f = 0,\ g = g_2$
$0 < x < h$	$f = \frac{f_1 x}{h},\ g = \frac{g_1 x}{h}$
$x > h$	$f = 0,\ g = \frac{g_1 x}{h},$

as follows:

When $x > h$, no links between actin and myosin have been made, and will not be made, since $f = 0$. Hence in this case, $n = 0$.

When $0 < x < h$, equation (28.6) is

$$-\frac{SV}{2}\frac{dn}{dx} = \frac{f_1 x}{h} - \left(\frac{f_1 x}{h} + \frac{g_1 x}{h}\right)n$$

$$= \frac{f_1 x}{h} - (f_1 + g_1)\frac{x}{h}n. \qquad (29.1)$$

The solution of this differential equation is the combined solution of a particular solution and the solution of the complementary or homogeneous equation. A particular solution occurs when n is a constant, then $\frac{dn}{dx} = 0$. Hence →

$$-\frac{SV}{2}\frac{dn}{dx} = 0 = \frac{f_1 x}{h} - (f_1 + g_1)\frac{x}{h} n,$$

and

$$n_p = \frac{f_1}{f_1 + g_1} . \tag{29.2}$$

The solution of the homogeneous equation,

$$-\frac{SV}{2}\frac{dn}{dx} = -(f_1 + g_1)\frac{x}{h} n \tag{29.3}$$

is found by arranging (29.3) as

$$\frac{dn}{n} = \frac{2(f_1 + g_1)}{SVh} x\, dx. \tag{29.4}$$

Integrating,

$$\ln n = \frac{f_1 + g_1}{SVh} x^2 + C.$$

Taking the log,

$$n_h = Ce^{\frac{(f_1 + g_1)x^2}{SVh}} . \tag{29.5}$$

Combining the particular solution, (29.2), with the solution of the homogeneous equation, (29.5), gives

$$n = \frac{f_1}{f_1 + g_1} + Ce^{\frac{(f_1 + g_1)x^2}{SVh}} . \tag{29.6}$$

The constant of (29.6) is evaluated by realizing that when $x = h$, $n = 0$. Thus, (29.6) becomes

$$0 = \frac{f_1}{f_1 + g_1} + Ce^{\frac{(f_1 + g_1)h}{SV}} , \tag{29.7}$$

and

$$C = -\frac{\frac{f_1}{f_1 + g_1}}{e^{\frac{(f_1 + g_1)h}{SV}}}$$

$$= -\frac{f_1}{f_1 + g_1} e^{-\frac{\phi}{V}}$$

where

$$\phi = \frac{(f_1 + g_1)h}{S}.$$

Therefore, substituting this value of C into (29.6) gives the complete solution:

$$n = \frac{f_1}{f_1 + g_1} - \frac{f_1}{f_1 + g_1} e^{-\frac{\phi}{V}} e^{\frac{(f_1 + g_1)x^2}{SVh}}$$

$$= \frac{f_1}{f_1 + g_1}\left(1 - e^{\frac{(f_1 + g_1)x^2}{SVh} - \frac{\phi}{V}}\right)$$

$$= \frac{f_1}{f_1 + g_1}\left(1 - e^{\left(\frac{x^2}{h^2} - 1\right)\frac{\phi}{V}}\right). \qquad (29.8)$$

When $x < 0$, equation (28.6) is written

$$-\frac{SV}{2}\frac{dn}{dx} = -g_2 n. \qquad (29.9)$$

Thus,

$$\frac{dn}{n} = \frac{2g_2}{SV}\,dx$$

and

$$\ln n = \frac{2g_2}{SV}x + C$$

and

$$n = Ce^{\frac{2g\,x}{SV}} . \tag{29.10}$$

Evaluating the constant of (29.10), realize from (29.8) that when $x = 0$,

$$n_{x=o} = \frac{f_1}{f_1 + g_1}\left(1 - e^{-\frac{\phi}{V}}\right). \tag{29.11}$$

Therefore, when $x = 0$, (29.10) becomes

$$n_{x=o} = \frac{f_1}{f_1 + g_1}\left(1 - e^{-\frac{\phi}{V}}\right) = C.$$

Substituting this value of C back into (29.10) gives the desired solution:

$$n = \frac{f_1}{f_1 + g_1}\left(1 - e^{-\frac{\phi}{V}}\right)e^{\frac{2xg_2}{SV}} . \tag{29.12}$$

In summary then, the three solutions of equation (28.6) are

$x > h$ $\qquad n = 0.$

$0 < x < h$ $\qquad n = \frac{f_1}{f_1 + g_1}\left(1 - e^{\left(\frac{x^2}{h^2} - 1\right)\frac{\phi}{V}}\right). \tag{29.8}$

$x < 0$ $\qquad n = \frac{f_1}{f_1 + g_1}\left(1 - e^{-\frac{\phi}{V}}\right)e^{\frac{2xg_2}{SV}} . \tag{29.12}$

Equation (28.9),

$$E = \frac{me}{L}\int_{-\infty}^{\infty} f(1 - n)\,dx, \tag{28.9}$$

may now be evaluated by inserting the above values for n. Writing (28.9) as

$$E = \frac{me}{L}\left[\int_{-\infty}^{\infty} f\,dx - \int_{-\infty}^{\infty} f\,n\,dx\right]$$

then

$$E = \frac{me}{L}\left[\int_0^h \frac{f_1 x}{h}\,dx - \int_0^h \frac{f_1 x}{h}\cdot\frac{f_1}{f_1+g_1}\left(1 - e^{\left(\frac{x^2}{h^2}-1\right)\frac{\phi}{V}}\right)dx\right]$$

$$= \frac{me}{L}\left[\frac{f_1 h}{2} - \frac{f_1}{h}\cdot\frac{f_1}{f_1+g_1}\cdot\frac{h}{2} + \frac{f_1}{h}\cdot\frac{f_1}{f_1+g_1}\int_0^h x\,e^{\left(\frac{x^2}{h^2}-1\right)\frac{\phi}{V}}\,dx\right]$$

$$= me\cdot\frac{h}{2L}\cdot\frac{f_1}{f_1+g_1}\left[f_1\left(\frac{f_1+g_1}{f_1}\right) - f_1 + \frac{2f_1}{h^2}\int_0^h x\,e^{\left(\frac{x^2}{h^2}-1\right)\frac{\phi}{V}}\,dx\right] \quad (29.13)$$

Since

$$f_1\left(\frac{f_1+g_1}{f_1}\right) - f_1 = g_1,$$

(29.13) can be written

$$E = me\,\frac{h}{2L}\cdot\frac{f_1}{f_1+g_1}\left[g_1 + \frac{2f_1}{h^2}\int_0^h x\,e^{\left(\frac{x^2}{h^2}-1\right)\frac{\phi}{V}}\,dx\right]. \quad (29.14)$$

The integral of (29.14) is evaluated as follows:

$$\int_0^h x\,e^{\frac{x^2\phi}{h^2V}-\frac{\phi}{V}}\,dx = \int_0^h x\,e^{\frac{x^2\phi}{h^2V}}\,e^{-\frac{\phi}{V}}\,dx = e^{-\frac{\phi}{V}}\int_0^h e^{\frac{x^2\phi}{h^2V}}\,x\,dx. \quad (29.15)$$

Letting $\frac{x^2\phi}{h^2V} = \mu$, then $d\mu = \frac{2x\phi}{h^2V}\,dx$ and $x\,dx = \frac{h^2V}{2\phi}\,d\mu$.

Substituting this value of x dx into (29.15),

$$= e^{-\frac{\phi}{V}} \int_o^h \frac{h^2 V}{2\phi} e^{\mu} \, d\mu$$

$$= e^{-\frac{\phi}{V}} \frac{h^2 V}{2\phi} e^{\mu} \Big|_o^h$$

$$= e^{-\frac{\phi}{V}} \frac{h^2 V}{2\phi} \left[e^{\frac{\phi}{V}} - 1 \right] = \frac{h^2 V}{2\phi} \left[1 - e^{-\frac{\phi}{V}} \right]. \qquad (29.16)$$

With this solution of the integral, (29.14) becomes

$$E = me \cdot \frac{h}{2L} \cdot \frac{f_1}{f_1 + g_1} \left[g_1 + f_1 \frac{V}{\phi} \left(1 - e^{-\frac{\phi}{V}} \right) \right]. \qquad (29.17)$$

In a similar fashion, equation (28.10),

$$P = \frac{msk}{2L} \int_{-\infty}^{\infty} n \, x \, dx, \qquad (28.10)$$

is evaluated.

Substituting into the equation the various values of n:

$$P = \frac{msk}{2L} \left[\int_{-\infty}^{\infty} \frac{f_1}{f_1 + g_1} \left(1 - e^{-\frac{\phi}{V}} \right) e^{\frac{2xg_2}{SV}} x \, dx + \int_o^h \frac{f_1}{f_1 + g_1} \left(1 - e^{\left(\frac{x^2}{h^2} - 1\right)\frac{\phi}{V}} \right) x \, dx \right]$$

$$= \frac{msk}{2L} \frac{f_1}{f_1 + g_1} \left[\int_{-\infty}^{o} \left(1 - e^{-\frac{\phi}{V}} \right) e^{\frac{2xg_2}{SV}} x \, dx + \int_o^h \left(1 - e^{\left(\frac{x^2}{h^2} - 1\right)\frac{\phi}{V}} \right) x \, dx \right]$$

$$= \frac{msk}{2L} \cdot \frac{f_1}{f_1 + g_1} \left[\int_{-\infty}^{o} e^{\frac{2xg_2}{SV}} x\,dx - \int_{-\infty}^{o} e^{-\frac{\phi}{V}} e^{\frac{2xg_2}{SV}} x\,dx + \int_{o}^{h} x\,dx \right.$$

$$\left. - \int_{o}^{h} e^{\left(\frac{x^2}{h^2} - 1\right)\frac{\phi}{V}} x\,dx \right]$$

$$= \frac{msk}{2L} \cdot \frac{f_1}{f_1 + g_1} \left[\int_{-\infty}^{o} x\, e^{\frac{2xg_2}{SV}} dx - e^{-\frac{\phi}{V}} \int_{-\infty}^{o} x\, e^{\frac{2xg_2}{SV}} dx + \frac{h^2}{2} \right.$$

$$\left. - e^{-\frac{\phi}{V}} \int_{o}^{h} x\, e^{\frac{x^2\phi}{h^2V}} dx \right].$$

For the first two integrals above, using the relation

$$\int x\, e^{ax}\, dx = \frac{1}{a^2} e^{ax} (ax - 1)$$

then

$$P = \frac{msk}{2L} \cdot \frac{f_1}{f_1 + g_1} \left[\frac{S^2V^2}{4g_2^2} e^{\frac{2xg_2}{SV}} \left(\frac{2g_2}{SV} - 1\right) \right|_{-\infty}^{o}$$

$$- e^{-\frac{\phi}{V}} \left(\frac{S^2V^2}{4g_2^2} e^{\frac{2xg_2}{SV}} \left(\frac{2g_2}{SV} x - 1\right) \right|_{-\infty}^{o} + \frac{h^2}{2}$$

$$\left. - e^{-\frac{\phi}{V}} \int_{o}^{h} x\, e^{\frac{x^2\phi}{h^2V}} dx \right]. \qquad (29.18)$$

The last integral is evaluated by letting

$$\mu = \frac{x^2\phi}{h^2V}, \quad d\mu = \frac{2x\phi}{h^2V} dx, \quad \text{and } x\,dx = \frac{h^2V}{2\phi} d\mu.$$

Thus the integral becomes

$$e^{-\frac{\phi}{V}} \int_0^h e^{\mu} \frac{h^2 V}{2\phi} d\mu = e^{-\frac{\phi}{V}} \frac{h^2 V}{2\phi} \cdot e^{\frac{x^2 \phi}{h^2 V}} \Bigg|_0^h = \frac{h^2 V}{2\phi} \left(1 - e^{-\frac{\phi}{V}}\right).$$

Equation (29.18) is therefore

$$P = \frac{msk}{2L} \cdot \frac{f_1}{f_1 + g_1} \left[\frac{S^2 V^2}{4 g_2^2} - e^{-\frac{\phi}{V}} \frac{s^2 V^2}{4 g_2^2} + \frac{h^2}{2} - \frac{h^2 V}{2\phi} \left(1 - e^{-\frac{\phi}{V}}\right) \right]$$

$$= \frac{msk}{2L} \cdot \frac{f_1}{f_1 + g_1} \cdot \frac{h^2}{2} \left[\frac{1}{2} \left(\frac{f_1 + g_1}{g_2} \right)^2 \frac{V^2}{\phi^2} \left(1 - e^{-\frac{\phi}{V}}\right) + 1 - \frac{V}{\phi} \left(1 - e^{-\frac{\phi}{V}}\right) \right]$$

or

$$P = \frac{msk}{2L} \cdot \frac{f_1}{f_1 + g_1} \cdot \frac{h^2}{2} \left[1 - \frac{V}{\phi} \left(1 - e^{-\frac{\phi}{V}}\right) \left(1 + \frac{1}{2} \left(\frac{f_1 + g_1}{g_2} \right)^2 \frac{V}{\phi} \right) \right], \qquad (29.19)$$

the desired solution.

The maximum work, w, that one site performs during one contraction is the product of the f, $kx_{x = h}$ or kh, and the relative distance the A and M sites move, or $\frac{h}{2}$. Hence, $w = kh^2/2$. The coefficient of (29.19) can accordingly be written

$$\frac{msw}{2L} \cdot \frac{f_1}{f_1 + g_1}.$$

The rate of doing mechanical work is the tension P times the velocity of shortening or PV. In terms of PV, equation (29.19) is written

$$\frac{ms\omega}{2L} \cdot \frac{f_1}{f_1 + g_1} V = m\omega \frac{hf_1}{2L} \cdot \frac{V}{\phi} .$$

Finally, the rate of liberation of heat, H, from the muscle is the rate of total energy liberation minus the rate of doing mechanical work, or

$$H = E - PV. \qquad (29.20)$$

EVALUATION OF HUXLEY'S ANALYSIS OF CONTRACTION

In the preceding chapters, equations were presented for the rate of energy liberation per cubic centimeter of muscle, for the total tension generated per centimeter^2 cross-sectional area of muscle, for the rate of doing mechanical work, and for the rate of liberating heat. These equations will now be fitted to experimental data.

Over twenty years ago, A. V. Hill determined certain relationships concerning the behavior of muscle. Two of these empirical relationships are:

1. The rate of liberation of heat increases linearly with the speed of shortening; i.e., the shortening heat is constant.

2. The total rate of energy liberation, work plus heat, increases linearly as the load is reduced below the isometric tension level.

As was discussed in a previous chapter, these relationships led to the Hill equation: $(P + a)(V + b) = \text{constant}$. The constant "a" was found to be equal to $\frac{1}{4}P_o$ (isometric tension), and "b" = $\frac{a}{P_o} v_{max}$.

Consider again equation (29.17),

$$E = m e \frac{h}{2L} \cdot \frac{f_1}{f_1 + g_1} \left[g_1 + f_1 \frac{V}{\phi} \left(1 - e^{-\frac{\phi}{V}} \right) \right]. \qquad (29.17)$$

When the velocity of shortening is zero, V = 0, then E = E_o, and is the rate of maintenance heat production:

$$E_o = me \frac{h}{2L} \cdot \frac{f_1 g_1}{f_1 + g_1} . \qquad (30.1)$$

Thus the rate of "extra" energy liberation with contraction, that above maintenance heat, is $E' = E - E_o$, or

$$E' = me \cdot \frac{h}{2L} \cdot \frac{f_1^2}{f_1 + g_1} \cdot \frac{V}{\phi} \left(1 - e^{-\frac{\phi}{V}}\right). \qquad (30.2)$$

In order to match these various equation with Hill's empirical data, the ratio of g_1/f_1 is chosen so that the rate of maintenance heat, equation (30.1), is about the same as found experimentally, and equal to ab. By trial and error, Huxley arrived at the following approximations:

$$g_1/f_1 + g_1 = 3/16$$

$$g_2/f_1 + g_1 = 3.919$$

$$\text{and a ratio of } w/L = 0.75$$

Using this data, then, the theoretical curves can be matched to Hill's empirical curves. Figure 30.1 shows the relationship between the speed of shortening and tension. The smooth line of the figure is a plot of Hill's equation, while the circles are a plot of

$$P = \frac{ms^w}{2L} \cdot \frac{f_1}{f_1 + g_1} \left[1 - \frac{V}{\phi}\left(1 - e^{-\frac{\phi}{V}}\right)\left(1 + \frac{1}{2}\left(\frac{f_1 + g_1}{g_2}\right)^2 \frac{V}{\phi}\right)\right]. \qquad (30.3)$$

In the theoretical plot, values of P are calculated for various values of V. The ordinate of the figure is the velocity as a fraction of

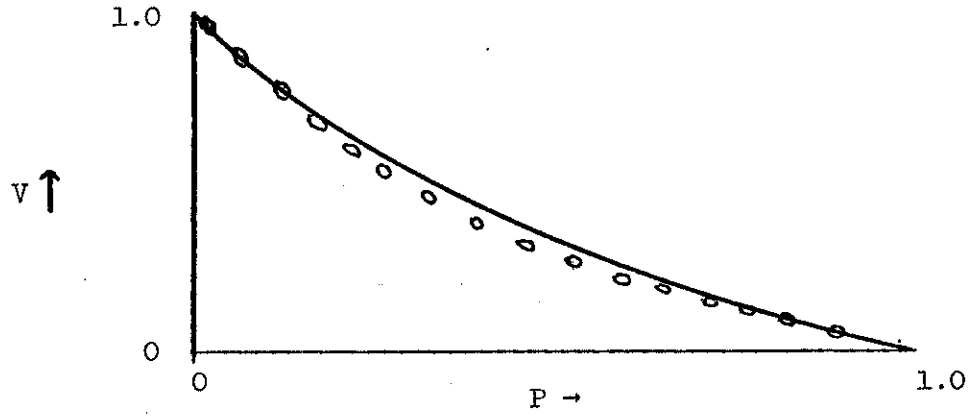


Figure 30.1 - Velocity of shortening vs. tension. Continuous line: Hill's data; circles: theoretical equation (30.3).

the value in unloaded tetanus, and the abscissa is the tension as a fraction of the value in isometric tetanus. The deviation of the theoretical plot from the experimental data is negligible.

Figure 30.2 shows the relation between the total rate of energy liberation, heat + work, and tension. Again the solid line is from Hill's data, while the circles represent a plot of equations (29.17) plus (30.3). On the abscissa scale, unity is P_o, and on the ordinate scale, unity is the product P_oV max.

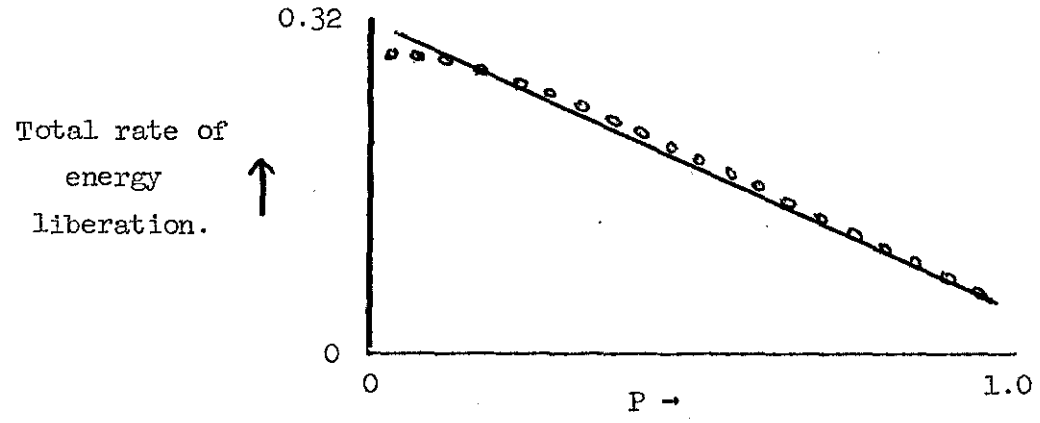


Figure 30.2 - Rate of Energy Liberation vs. Tension.

Figure 30.3 further illustrates the closeness of the fit between experimental and theoretical plots. Here the relationship of rate of heat production to speed of shortening is shown. The ordinate scale is as in Figure 30.2, while unity on the abscissa scale is V max., the speed of shortening in an unloaded tetanus.

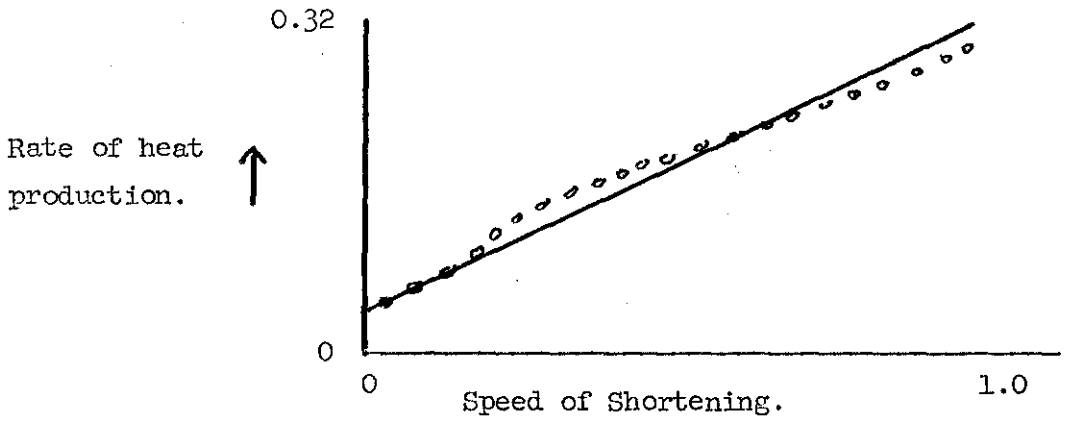


Figure 30.3 - Rate of Heat Production vs. Speed of Shortening. Solid line: Hill's data; circles from equation (29.20).

Finally, Figure 30.4 shows the relationship between the total rate of energy liberation and the speed of shortening. The scales are the same as in Figure 30.3, and the solid line is derived from Hill's relationships. The circles are calculated from equation (29.17).

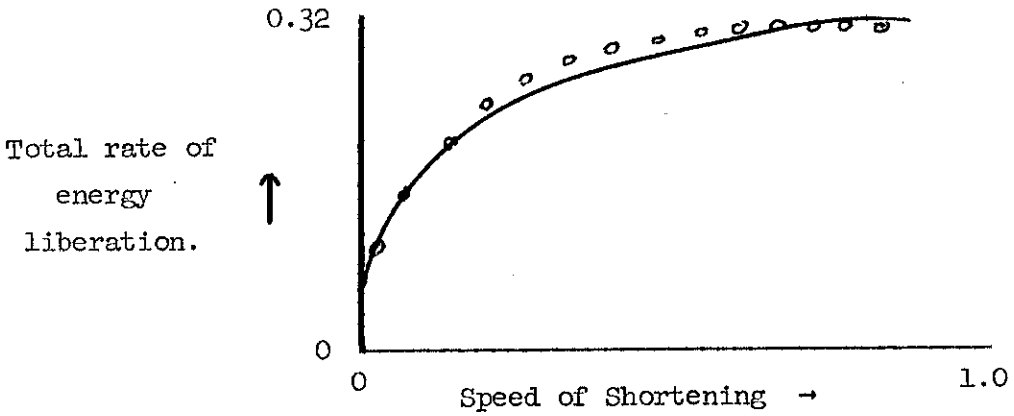


Figure 30.4 - Total Rate of Energy Liberation as a Function of the Velocity of Contraction.

As can be seen from Figures 30.1 through 30.4, the fit of the theoretical equations with actual behavioral data is not exact, but probably within the experimental error with which the data was collected. One improvement on the theory may be to alter the relationships of f and g to x. Other relationships have been tried, such as rendering f and g constant, or having f and g vary exponentially with x. Such efforts, however, have proven unprofitable.

The assumptions defining the function of f and g with x may seem at first glance to be unreasonable. However, with these assumptions, the

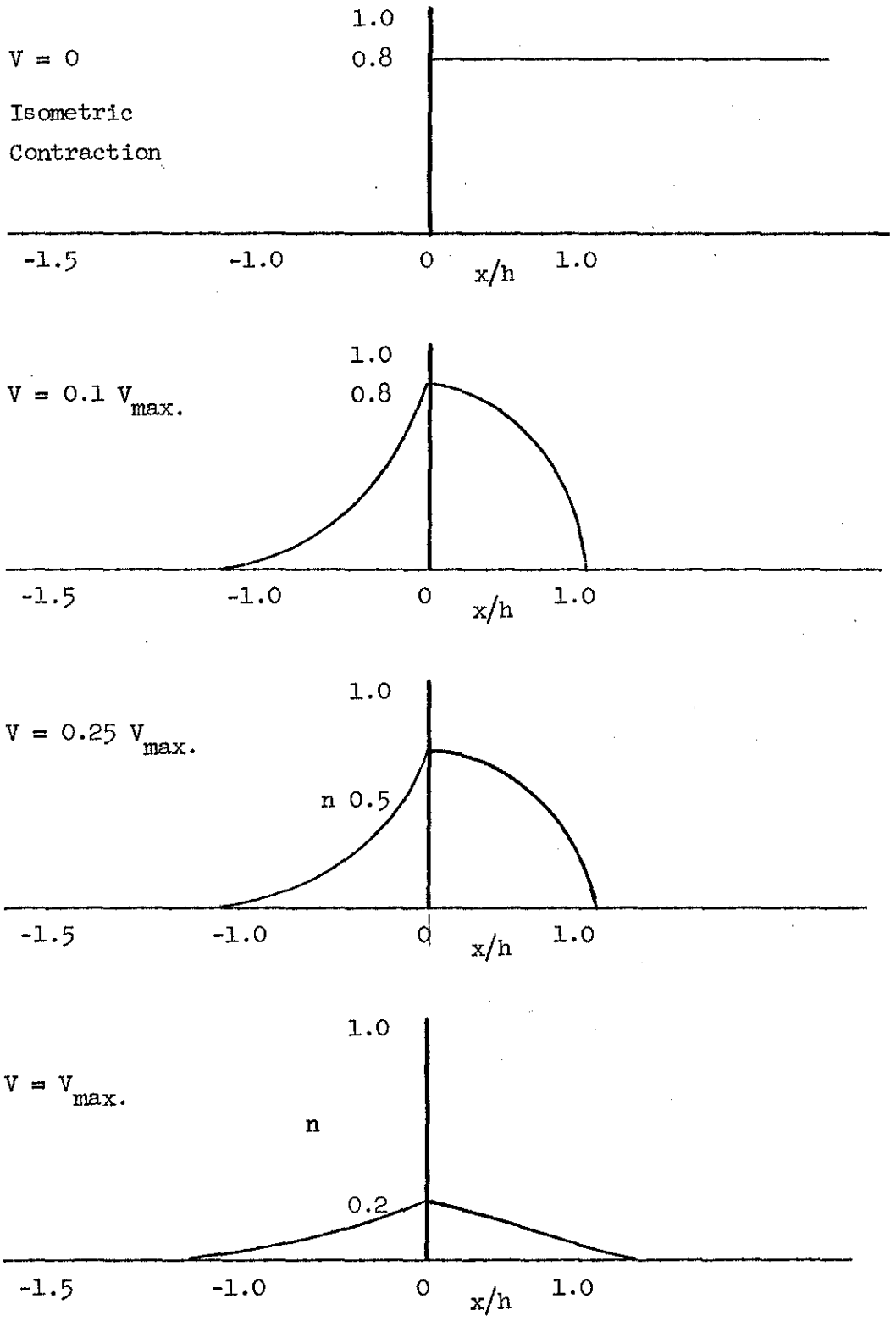


Figure 30.5 - Variation of n (proportional of sites at which links between actin and myosin are in existance) with x (position of A site to M site = 0, for four different shortening speeds.

manner in which n varies with x is not unreasonable. Figure 30.5 shows the values of n, calculated from $n = 0$ at $x > h$, and from equations (29.8) and (29.12), for four different speeds of shortening. Thus, during isometric contraction, with $V = 0$, the proportion of sites formed remains constant regardless of the length of the muscle. During shortening, the proportion of sites rises rapidly from zero at h, to a maximum value at $x = 0$, then falls off extremely fast to zero at minus values of x. As the velocity of contraction approaches the maximum, $V_{max.}$, the proportion of the linked sites decreases, as one would expect, and the breaking of the links is also retarded. Thus the assumptions behind f, $g = f$, $f'(x)$ becomes more profitable. For further discussion of this theory, the reader should consult the writings of A. F. Huxley.

At this point the book is concluded. With the work of Podolsky and Huxley, the reader is brought to the frontier of knowledge about muscle. If the present day hypotheses seem inadequate, which they are, one should keep in mind ~~two points. First,~~ that future hypotheses will not be easily conceived, ~~and second, just reading a book about muscle is really~~ nothing ~~more than a form of idleness.~~